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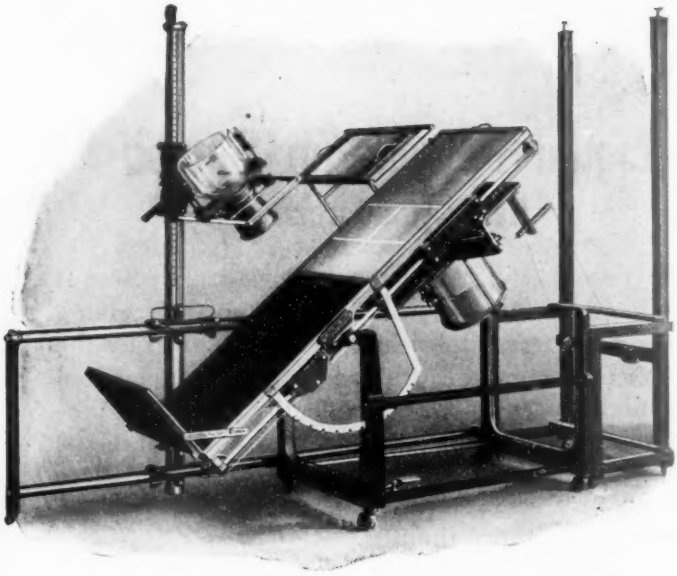

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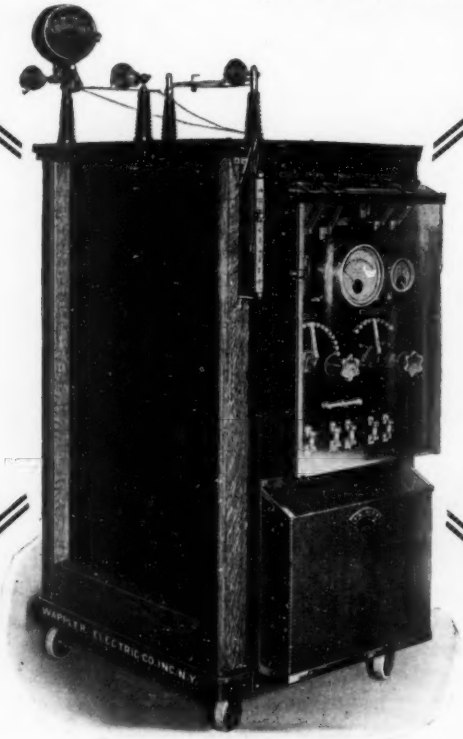

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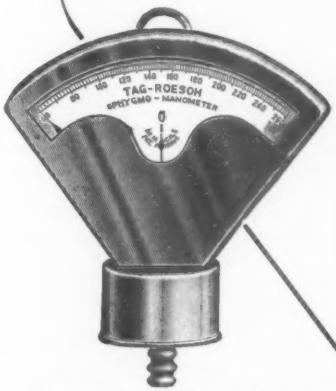

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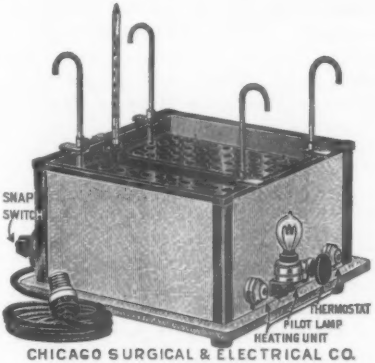

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ORIGINAL ARTICLES

SENSITIZED VACCINES IN THE PROPHYLAXIS AND TREATMENT OF INFECTIONS.

By Russell L. Cecil, M.D., Major, U. S. M. R. C.,
NEW YORK CITY.

(From the Second Medical Service of Bellevue Hospital and the Medical Department of Cornell University, New York.)

A SENSITIZED vaccine is a suspension of bacteria which has been previously treated with an homologous serum. The administration of sensitized vaccine has sometimes been referred to as serovaccination or "combined active-passive immunization." Both of these terms are misleading: the former because the serum is removed by washing the bacteria before they are injected, the latter for the reason that the immunity produced is probably entirely active. Whatever antibody is present in the vaccine is firmly attached to the bacteria, and whatever value sensitization of a vaccine possesses probably inheres from the direct influence of the antibody on the bacteria to which it is attached.

Vaccination with a mixture of serum and vaccine has, of course, been tried by a number of investigators. Shiga[1] used such a mixture for immunizing against plague and dysentery. Calmette and Guerin[2] produced a considerable degree of protection against the bovine tubercle bacillus in cattle that had been inoculated with a mixture of bovine tubercle bacilli and immune (?) serum. Leclainche[3] has used this method for vaccinating against erysipelas.

[1] Deutsch. med. Wchnschr., 1901, xxvii, 741.
[2] Compt. rend. Acad. sc., 1910, cli, 32.
[3] Revue veterinaire, 1900, xxv.

Sensitized vaccines in the true sense of the word were first employed in 1902 by Besredka.[4] He experimented with sensitized plague and typhoid bacilli which had been killed by heat, and found that the sensitized bacilli, both subcutaneously and intraperitoneally, were considerably less toxic than the non-sensitized bacilli; furthermore, that injections of sensitized bacilli were followed by an almost *immediate* increase in immunity, in contrast to the non-sensitized bacteria which excited first a so-called "negative phase."

In 1911 Metchnikoff and Besredka[5] succeeded in reproducing typhoid fever in chimpanzees by feeding them the excreta from a case of human typhoid fever. These investigators then experimented with various methods of vaccinating apes against typhoid. They found that killed typhoid bacilli, sensitized or non-sensitized, did not confer a sure and certain protection against typhoid fever in the chimpanzee. Living bacilli, however, if sensitized, produced a high immunity. The next experiment was to test the living sensitized bacilli on human beings. When one or two one-hundredths of a gelatin culture of living sensitized typhoid bacilli were injected subcutaneously a small area of erythema, slightly tender, developed at the site of the inoculation, but the temperature remained normal and the patient showed no untoward symptoms. In a later study the same experimenters showed that the blood and urine remained sterile even after large doses of living sensitized typhoid bacilli had been injected subcutaneously.

Besredka[6] has more recently reported his results with the use of living sensitized typhoid vaccine in human beings. On the island of Braqueville about one-half of the 930 inhabitants were vaccinated while the other half served as controls. During the year following four controls developed typhoid fever, while of those vaccinated all escaped infection.

In England, Broughton-Alcock[7] has used living sensitized typhoid vaccine in 750 cases for prophylactic purposes. His experience was similar to that of Besredka. A slight local reaction was obtained, but the temperature was rarely increased and other constitutional symptoms were entirely absent.

Sawyer[8] has recently reported the results of antityphoid vaccination in the State of California, and gives comparative figures for sensitized and non-sensitized vaccine. In the first place he found that there was little difference between the vaccines in regard to the severity of the reactions produced. Out of 2906 cases vaccinated with the sensitized vaccine 4.3 per cent. later developed typhoid; whereas in 4967 cases vaccinated with non-sensitized vaccine there was 6.9 per cent. of failures. Hence the percentage of failures indicates a slight advantage for the sensitized vaccine, though as the

[4] Ann. de l'Inst. Pasteur, 1902, xvi, 918.
[5] Ibid., 1911, xxv, 193, 867; 1913, xxvii, 597.
[6] Ibid., 1913, xxvii, 607.
[7] Lancet, 1912, clxxxiii, 504; 1913, clxxxiv, 1155.
[8] Jour. Am. Med. Assn., 1915, lxv, 1413.

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authors point out, the two sets of statistics are not exactly comparable.

Gay and Claypole[9] have published an interesting experimental study on the various methods of prophylactic vaccination against typhoid infection in rabbits: (1) they found that unsensitized bacteria killed and precipitated by alcohol do not protect so well as sensitized typhoid bacilli treated in the same manner; (2) they showed that the alcohol-killed sensitized cultures protect almost as well as living sensitized cultures and that the sediment of alcohol-killed sensitized cultures gives a better protection than living sensitized cultures. Moreover, they found that the sensitized cultures produced little or no reaction in human beings. They recommend the dried ground sensitized sediment for vaccination against typhoid fever in human beings and give the three injections at two-day intervals in doses equivalent to 750,000,000 typhoid bacilli.

More recently the sensitized vaccine of Besredka has been extensively tried as a therapeutic measure in typhoid fever. Ardin, Delteil, Negre and Raynoud,[10] for example, employed it in 48 cases and had only one death (2.08 per cent.). Garbat[11] has reported his experience with sensitized typhoid vaccine in the treatment of 17 cases of typhoid fever. He concludes that in vaccinated patients the disease runs a milder course and complications are less frequent.

Ichikawa[12] reports a series of 82 cases of typhoid fever treated with living sensitized vaccine administered intravenously. There were 9 deaths (a mortality of 11 per cent.). The author claims that the usual mortality for this disease in the hospital where he worked was about 30 per cent. He also tried the vaccine subcutaneously on 23 cases, with indifferent results.

Gay and Chickering[13] treated 53 cases of typhoid fever with intravenous injections of a sensitized killed typhoid vaccine sediment prepared by the method of Gay and Claypole already described. The intravenous injection of the vaccine nearly always produced a chill, rise and fall of temperature and leukopenia followed by hyperleukocytosis. The injection of the vaccine was followed in a number of cases by the disappearance or diminution of bacteriemia and usually by an increase in the Widal. The mortality in this series was 9 per cent., or just about that of the best hospitals. In 66 per cent. of the cases a distinct benefit was obtained, as showed by lower temperature, disappearance or amelioration of subjective symptoms and an apparently accelerated recovery.

Although vaccination with sensitized virus has been mostly studied with the typhoid bacillus its use has not been confined to this organism. In both France and England sensitized gonococcus

[9] Arch. Int. Med., 1914, xiv, 671; Jour. Am. Med. Assn., 1913, lx, 1950.
[10] Ann. de l'Inst. Pasteur, 1913, xxvii, 644.
[11] Jour. Am. Med. Assn., 1915, lxiv, 489.
[12] Ztschr. f. Immunitätsf., 1914, xxiii, 32.
[13] Arch. Int. Med., 1916, xvii, 303.

vaccine has been extensively employed as a therapeutic measure with apparently gratifying results. Dopter and Pauron[14] found that gonorrheal arthritis and orchitis responded quickly to sensitized gonococcus vaccine. According to Broughton-Alcock, sensitized gonococcus vaccine was of no value in acute urethritis, but in arthritis, orchitis and epididymitis its effects were brilliant. Nicolle and Blaizot[15] have also obtained good results in gonorrheal infections with sensitized gonococcus vaccine.

Sensitized streptococcus vaccine was first employed by Levy and Hamm.[16] They treated 8 cases of puerperal fever with the autogenous bacteria, killed with carbolic acid and sensitized with a polyvalent streptococcus-immune serum. Six of the 8 cases recovered. Marxer found that sensitized streptococci killed with galactose were more efficient for protecting rabbits against streptococcus than were the killed unsensitized organisms. Broughton-Alcock has tried sensitized living streptococci as a therapeutic agent in impetigo, suppurative lymphadenitis, pyorrheas and sinusitis and claims to have obtained remarkable results. He sensitized the bacteria with a polyvalent antistreptococcus serum.

In 1910 Levy and Aorki[17] found that sensitized pneumococcus vaccine gave rabbits a higher degree of protection against the pneumococcus than ordinary vaccine and that its administration was not followed by a negative phase. According to their experiments the sensitized vaccine (killed by 0.5 per cent. carbolic) was less toxic than the non-sensitized, an observation in accord with that made by other observers in the case of various bacteria. As to its curative effect, it was absolutely useless if injected later than a few minutes after the administration of ten times the lethal dose. When the two were injected simultaneously some of the animals were saved.

Swift and Kinsella[18] have found that the serum of rabbits which have been injected with sensitized Streptococcus viridans, either dead or living, does not contain agglutinins, complement-fixation antibodies or protective antibodies. Similar results were obtained with sensitized vaccines of pneumococci, but sensitized living pneumococci showed a rapid production of antibodies.

Swift and Kinsella[19] have lately studied active immunization with sensitized pneumococci. In mice there was practically no difference in the degree of active immunity conferred by plain and sensitized vaccine. In guinea-pigs the sensitized vaccine was less efficacious than the plain. In rats there was also a higher degree of immunity in the plain vaccine series, but the immunity produced by the sensitized vaccine persisted longer.

These authors also show that animals may possess a high degree

[14] Bull. et mém. Soc. méd. des hôp. de Paris, 1913, xxxvi, 386.
[15] La Semaine Méd., 1913, xxxiii, 497, 595.
[16] München. med. Wchnschr., 1909, lvi, 1728.
[17] Ztschr. f. Immunitätsf. u. exper. Therapie, 1910, vii, 435.
[18] Proc. Soc. Exper. Biol. and Med., 1915–16, xiii, 103.
[19] Ibid., 1916–17, xiv, 120.

of active immunity and still show practically no antibodies in their serum, and they suggest that the immunity may be due in part to a tissue immunity.

Broughton-Alcock resorted to sensitized Staphylococcus aureus vaccine in a series of cases that had not responded well to unsensitized vaccine and obtained excellent results. He had the courage to employ a living vaccine, and in the earlier part of his work produced a number of abscesses at the site of inoculation.

Von Behring[20] has recently introduced a method of active immunization against diphtheria which consists in vaccinating human beings with a diphtheria toxin that has been neutralized with antitoxin.

A so-called "sensitized" tuberculin was first introduced by Fritz Meyer[21] in the form of a sensitized bacillary emulsion. Meyer found that (1) tuberculous animals could stand five times as much sensitized tuberculin as unsensitized; (2) that healthy animals could stand numerous injections of the sensitized vaccine, while they died after repeated injections of unsensitized tuberculin; (3) that healthy animals which could not be immunized with dead bacilli, developed so much resistance after a long treatment with sensitized material that a subsequent infection was much milder and ran a course six to eight times longer than the controls; (4) that freshly tuberculous animals by treatment with sensitized tuberculin got so much better that they could be looked upon as cured.

Meyer treated 47 cases of pulmonary and local tuberculosis with sensitized tuberculin, and of these 40 showed more or less improvement. The best results were obtained in the localized infections. In the pulmonary cases there was an improvement in the symptoms, but the signs in the chest and the bacilli in the sputum persisted. Citron[22] has also worked with sensitized tuberculin and looks upon it with favor. Both Meyer and Citron emphasize the mildness of the local reaction as compared with that of the usual bacillary emulsion.

During the past two years I have had some experience with sensitized vaccines, enough perhaps to justify a brief report of the results which I have obtained. I have employed sensitized vaccines of the typhoid bacillus, gonococcus, streptococcus, Staphylococcus aureus and tubercle bacillus. In the case of the typhoid bacillus the vaccine has been used only for prophylaxis, whereas with the other bacteria the vaccines were employed for therapeutic purposes. The technic of preparation of the various vaccines will be described separately.

1. Sensitized Typhoid Vaccine. My experience with sensitized typhoid vaccine has been limited to 20 cases, in which it was used for prophylaxis. The vaccine was prepared from a stock strain

[20] Berl. klin. Wchnschr., 1914, li, 917.
[21] Ibid., 1910, xlvii, 926.
[22] Ibid., 1909, xlvi, 2288.

of Bacillus typhosus which had been under cultivation for several years in the laboratory. The bacteria were grown, as usual, on plain agar, washed off with normal salt solution, shaken, standardized and killed by heating at 56° for one hour. The killed bacteria were then treated with an excess of inactivated serum obtained from rabbits immunized against the homologous strain. The suspension was incubated in the water-bath for two hours, centrifuged, washed twice with normal saline and made up to the original volume. The dosage employed in all these cases was the same as that usually employed with ordinary typhoid vaccine, namely, 500,000,000 for the first inoculation and 1,000,000,000 each for the second and third. In 8 of the cases the vaccine was given at seven-day intervals; in the remaining 12 cases it was administered every other day, according to the method of Gay and Claypole. The latter method has the advantage in economy of time and seems to cause no unpleasant symptoms.

It will be observed that in this vaccine the bacteria were killed with heat, in this respect differing from that of Besredka and others who have used the living organism. It seemed to me that the slightly superior immunizing quality of the living vaccine was not a sufficient advantage to justify the risk involved in using the living organism.

The local reaction produced by the sensitized vaccine was always mild—less severe, I think, than that which usually follows an injection of ordinary typhoid vaccine. The area of induration and hyperemia was less extensive and the tenderness not so marked or persistent. The constitutional reaction was generally negligible. Occasionally a slight frontal headache or a feeling of lassitude was noticed a few hours after the vaccine was injected, but these symptoms soon passed away. One patient had a low grade of fever for several weeks after receiving the second inoculation and developed a slight cough and signs at the left apex. A diagnosis of pulmonary tuberculosis was made, though the tubercle bacillus was never found. She had been vaccinated against typhoid just one year previously. Under appropriate treatment she made a gradual but complete recovery.

The results of Gay and Claypole's experimental study of typhoid septicemia in rabbits give considerable weight to the presumption that in human beings sensitized typhoid vaccine would confer a higher immunity against typhoid fever than the unsensitized vaccine gives. This point, however, is at present incapable of final demonstration. It has been shown by Besredka and his co-workers that sensitized typhoid bacilli stimulate agglutinin formation to a less marked degree than non-sensitized bacilli, but that, on the other hand, phagocytosis and bacteriolysis are much more active after vaccination with the sensitized organisms.

The superiority of sensitized over non-sensitized typhoid vaccine in immunization against typhoid fever can be established only by an extensive use of the former and a comparison of the results with

those which have been obtained by non-sensitized vaccine. In the meanwhile the lesser toxicity of the sensitized vaccine and its possibly superior immunizing power are sufficient reasons for giving it a thorough trial.

2. Sensitized Gonococcus Vaccine. I have employed sensitized gonococcus vaccine in 16 cases of gonococcus infection; gonorrheal vaginitis uncomplicated, 4 cases; vaginitis with endometritis, 1 case; vaginitis with salpingitis, 2 cases; vaginitis with arthritis, 2 cases; vaginitis with pregnancy, 2 cases; vaginitis, arthritis and pregnancy, 1 case; gonorrheal arthritis, 3 cases; gonorrheal epididymitis, 1 case. The gonococcus vaccine used was a stock vaccine prepared from the ten strains of the New York City Board of Health. The bacteria were cultivated on veal agar and sensitized in the living state with serum from a horse immunized against the homologous strains. The general method of preparation was similar to that employed in the case of typhoid vaccine, with the exception that the bacteria were not killed. They unquestionably died, however, very shortly after the vaccine was prepared, as they were suspended in salt solution which contained 0.5 per cent. phenol.

Of the 12 cases of gonorrheal vaginitis only 1 was an infant; the ages varied from three to twenty-nine years. By referring to Table 1 it will be seen that 2 of these cases were complicated by gonorrheal salpingitis and 2 others by gonorrheal arthritis. In every case the infection was several weeks or months old before vaccination was started. The inoculations were given at intervals of five to ten days; the average number of inoculations were nine, but 1 case received as many as sixteen. An interesting feature in connection with this series is the size of the doses. On reference to the table it will be seen that the dosage varied from 100,000,000 to 2,000,000,000, the former being usually the initial dose. These doses are, of course, much larger than those usually given of ordinary gonococcus vaccine. The reactions, as a general rule, were mild; in nearly every case the first inoculation excited a sharp local reaction, but the following injections rarely caused much inconvenience or pain. There was only one definite constitutional reaction, that was in Case 9, where after the second inoculation of 200,000,000 the patient had a headache and fever and was nauseated. Six of these cases recovered completely; 4 others showed improvement and they were lost sight of; the remaining 2 cases showed no improvement. It is difficult to say in these cases just how much benefit the patients derived from the vaccines, as they were receiving at the same time local treatment in the form of vaginal douches of potassium permanganate and weekly vaginal distention of 5 per cent. silver nitrate. These patients were not considered cured until vaginal smears were entirely free of gonococci and practically free of pus cells. In Cases 2 and 3 the vaginitis was complicated by pyosalpinx. In both these cases the local pain and tenderness subsided and almost disappeared during the course of the vaccine treatment.

TABLE OF CASES TREATED WITH SENSITIZED VACCINES.

GONOCOCCUS CASES.

	Age, yrs.	Diagnosis.	Duration of infection before vaccine treatment.	Number of inoculations.	Dosage.	Character of reactions.	Other treatment employed.	Result.
No. 1	21	Gon. vaginitis	3 weeks	10	100 to 1000 million	Usually mild; one sharp reaction, after sixth inoculation	Five per cent. silver nitrate; vaginal distentions	Complete recovery; vaginal smears negative.
No. 2	29	Gon. vaginitis; gon. salpingitis	7 months	16	200 to 2000 million	Arm quite sore after first and second inoculations; other reactions mild	$AgNo_3$ vaginal distentions; lacto-bacilline douche; ichthyol tampon	Complete recovery from vaginal discharge; smears and gonorrhea-fixation test negative; still slightly tender over right tube when last seen.
No. 3	21	Gon. vaginitis; gon. salpingitis	6 weeks	12	100 to 800 million	All mild	$AgNo_3$ vaginal distentions; potassium permanganate douche	Recovery from vaginal discharge; smears negative; disappearance of tenderness and pain over right tube.
No. 4	16	Gon. vaginitis; pregnancy	3 months	7	200 to 1000 million	Slight nausea after fourth dose; several sharp local reactions	$AgNo_3$ vaginal distentions	Successful delivery of child at full term during course of treatment; lost sight of; when last seen slight vaginal discharge but no gonococci.
No. 5	29	Gon. vaginitis	1 month	6	100 to 500 million	One severe reaction after fourth inoculation; others mild	Potassium permanganate douches	Recovered; vaginal smears negative.
No. 6	3	Gon. vaginitis	2 months	12	100 to 1200 million	All mild	Boric acid douches	Recovered; vaginal smears negative.
No. 7	23	Gon. vaginitis; gon. arthritis	Vaginal discharge 2 years; arthritis 3 months	2	100 to 200 million	Mild	Vaginal douches	Improved, slightly; lost sight of.
No. 8	28	Gon. vaginitis	12 months	15	100 to 2000 million	Mild	$AgNo_3$ vaginal distentions; vaginal douches	Recovered; vaginal smears and gonorrhea-fixation test negative.
No. 9	26	Gon. vaginitis; gon. arthritis; pregnancy	5 months	15	100 to 1000 million	Slight constitutional reaction after second inoculation; mild local reactions	Vaginal douches	Vaccine discontinued at end of eighth month of pregnancy; complete recovery from arthritis; practically no vaginal discharge; successful delivery one month later.
No. 10	22	Gon. urethritis; gon. vaginitis; gon. endometritis	11 months	8	100 to 500 million	Several sharp local reactions	$AgNo_3$ vaginal distentions; potassium permanganate douches	Improved; lost sight of.
No. 11	15	Abortion; gon. vaginitis	7 months	8	100 to 600 million	Several severe local reactions	$AgNo_3$ vaginal distentions; potassium permanganate douches	Slight if any improvement; irregular in attendance at clinic.
No. 12	18	Gon. vaginitis; gon. arthritis	9 months	7	100 to 400 million	Reactions generally severe	$AgNo_3$ vaginal distentions; potassium permanganate vaginal douches	No improvement; poorly nourished; general health poor; arthritis slightly better when last seen.
No. 13	35	Gon. arthritis (chronic)	2 years	5	100 to 300 million	Mild	Baking and massage	No improvement; patient lost sight of after fifth inoculation.
No. 14	21	Gon. urethritis	3 months	11	100 to [illegible] million	[illegible]	[illegible]	[illegible]

No. 14	21	Gon. urethritis; gon. arthritis	3 weeks	11	10 to 2000 million	Patient had sharp rise of temperature and was irrational for a short time after 2000 million dose	Baking and massage; first five inoculations were ordinary gonorrheal vaccine	Arthritis lasted three months; complete recovery.
No. 15	22	Gon. arthritis; gon. urethritis	2 weeks	16	30 to 1000 million	Mild	Baking and massage; prostatic massage	Complete recovery after three months' treatment; first eight inoculations ordinary vaccine; last eight sensitized.
No. 16	21	Gon. epididymitis	11 days	11	200 to 1000 million	Mild	Suspensory and poultices	Recovery ten days after institution of vaccine treatment.
STREPTOCOCCUS CASES.								
No. 1, C. L.	16	Chronic infectious endocarditis	3 months	11	100 to 800 million	Mild	Transfused once with blood from an immunized donor	Died from acute nephritis.
No. 2, H. L.	42	Chronic infectious endocarditis; alveolar abscess	Several months	6	5 to 50 million	Mild	First four injections were ordinary autogenous vaccine	Died.
No. 3, D. K.	22	Chronic infectious endocarditis	6 weeks	8	40 to 600 million	One constitutional reaction (?); others mild	None	Died; duration of illness three and one-half months.
No. 4, M. G.	24	Chronic infectious endocarditis	Several months	3	100 to 400 million	Mild	None	Died.
No. 5, T. K.	21	Acute cervical lymphadenitis; acute arthritis; streptococcus septicemia	3 weeks	9	200 to 2000 million	One constitutional reaction following 2 billion dose	Sodium salicylate; aspiration and irrigation of knee-joint	Recovered after three months' illness.
STAPHYLOCOCCUS AUREUS CASE.								
No. 1, Mr. K.	35	Furunculosis	1 year or more before sensitized vaccine was used	4	10 to 100 million	Mild	Surgical treatment when indicated	Permanent recovery.
TUBERCULOUS CASES.								
No. 1, A. G.	15	Tuberculous adenitis	Several months	15	0.000001 c.c. to 0.0007 c.c. S. B. E.	One sharp local reaction; several focal reactions	Fresh air; diet	Apparently complete recovery; glands disappeared.
No. 2, M.	49	Tuberculous adenitis (recurrence after operation)	5 years	18	0.000001 c.c. to 0.01 c.c. S. B. E.	Two sharp local reactions	Staphylococcus aureus vaccine for discharging sinus	Glands disappeared; slight discharge from sinus has almost disappeared after Staphylococcus aureus vaccination.
No. 3, S. G.	7	Tuberculous adenitis	1 year	14	0.000001 c.c. to 0.0003 c.c. S. B. E.	Mild reactions	Eventual excision of glands	No improvement; one large gland became fluctuant; excision; recovery.
No. 4, B. D.	23	Tuberculous adenitis	10 years	10	0.00001 c.c. to 0.0005 c.c. S. B. E.	Mild reactions	Fresh air; diet; *x*-ray	Glands became smaller but did not disappear.
No. 5, V.	28	Tuberculosis of the vertebræ	5 years	2	0.0000005 c.c. to 0.000001 c.c. S. B. E.	Marked rise of temperature after both injections	Psoas abscess drained	Patient so sensitive to tuberculin that only the two injections were given; patient died a few months later.

Gonococcus Epididymitis. Sensitized vaccines have been used in only 1 case of gonorrheal epididymitis. Case 16 received his first dose of vaccine eleven days after the onset of the epididymitis. At that time swelling and pain were both marked. Three days later the swelling was much reduced and the acute symptoms had disappeared and a second dose was administered; three days later the swelling was gone and the testicle was practically normal. After two more inoculations the patient was declared cured. The only local treatment used was a flaxseed poultice and a suspensory.

Gonococcus Arthritis. Five cases of gonococcus arthritis were treated. Two of these were associated with gonorrheal vaginitis, 3 with gonorrheal urethritis. The first case of the gonorrheal vaginitis series (No. 9) had an arthritis of the right ankle. After five doses of vaccine the symptoms in the joint had entirely disappeared, though the vaginal discharge continued for some time after. In Case 14 there was polyarthritis following acute urethritis. This patient received several doses of ordinary stock gonococcus vaccine. After one month of local treatment and vaccination with stock vaccine, vaccination with sensitized vaccine was started. Large doses were given every five or six days, the largest being 2,000,000,000. After two months' treatment the patient was discharged free from symptoms. In Cases 7 and 13 the patients were lost sight of before the treatment was completed. The former showed improvement after two injections of vaccine; the latter felt no better after five injections. The fifth case (No. 12) of the gonorrheal series showed very little improvement of either condition; she was a poorly nourished, neurotic girl and was irregular in her attendance at the clinic.

In summarizing the gonococcus infections treated with sensitized vaccine, one received the impression that the vaccine has been of some benefit in most instances, but the results are no better than those obtained with ordinary vaccine. The 2 cases of vaginitis which failed to respond to treatment were both poorly nourished women of a type that never reacts particularly well to vaccine treatment of any kind.

3. Sensitized Streptococcus Vaccine. I have employed sensitized streptococcus vaccine in 5 cases; 4 of these were cases of chronic infectious endocarditis; the fifth was a case of streptococcus septicemia. In all of these cases living autogenous streptococcus vaccine was used and the serum employed for sensitizing the bacteria was that of rabbits immunized against the homologous strain.

(*a*) *Infectious Endocarditis.* These were all typical cases of infectious endocarditis of several months' duration, and they all showed Streptococcus viridans in blood culture. Case 1 received in addition to the sensitized vaccine a transfusion from a donor who had also been inoculated with the same vaccine. The only effect

exhibited in any of these cases was a slight temporary reduction of temperature for two or three days following the injection, and even this reaction was not constant. All four patients died.

(*b*) The fifth case was one of Streptococcus septicemia, and is so interesting that I shall describe it in detail.

K. T., male, aged twenty-one years, student. Eight days before admission patient was suddenly taken with sore throat, headache, fever. Diagnosis: acute tonsillitis. After three days the sore throat subsided, but glands in the neck became swollen and tender. Patient was seen by Dr. Blake, who advised incision of the glands.

May 10, 1913. Glands incised by Dr. Blake; pus removed.

May 12. Temperature, 105°; chill, nausea, vomiting; blood culture shows a streptococcus which produces a slight hemolysis.

May 14. 200 c.c. antistreptococcus serum.

May 16. 25,000,000 autogenous streptococcus vaccine.

May 18. 50,000,000 autogenous streptococcus vaccine.

May 19. 175 c.c. antistreptococcus serum followed by a chill.

May 20. Blood culture Streptococcus hemolyticus; no signs of endocarditis.

May 25. 170 c.c. antistreptococcus serum followed by symptoms of anaphylactic shock and urticaria.

May 29. 200,000,000 autogenous living *sensitized* streptococci.

May 30. Temperature high and steady; patient moved to the country.

June 1. Pain in the right knee.

June 2. Signs of fluid in the right knee.

June 3. 400,000,000 sensitized vaccine given.

June 6. 100 c.c. cloudy, sticky fluid aspirated from the right knee.

June 8. Temperature, 105°; two chills; pulse poor; cultures from knee; Streptococcus hemolyticus.

June 10. 30 c.c. purulent fluid removed from joint.

June 11. Patient given sodium salicylate, 30 grains t. i. d.

June 13. Sensitized vaccine, 600,000,000.

June 16. Sensitized vaccine, 800,000,000.

June 17. Knee-joint irrigated with phenol solution, 1 to 80.

June 18. Chill; temperature, 106°.

June 20. Knee aspirated and irrigated; profuse sweating.

June 21. Knee aspirated; chill; temperature, 103°.

June 23. Chill.

June 24. Knee aspirated.

June 26. Knee aspirated; fluid decreasing and thinner.

June 27. 800,000,000 vaccine.

June 28. Knee aspirated; white blood cells, 14,200.

June 29. Knee aspirated; chilly; temperature, 104°.

June 30. Knee aspirated; 1 fluidounce removed; temperature, 105°.

July 1. Knee aspirated.
July 2. Vaccine, 1,000,000,000.
July 3. Knee aspirated; temperature, 99° at 9 A.M.; no chill.
July 4. Phenol, 1 to 120; temperature, 99° to 100°.
July 5. One fluidounce removed; temperature, 99.6° to 100.3°.
July 9. Aspiration discontinued; vaccine, 1,500,000,000; temperature normal.
July 10. Temperature, 102°; vaccine, 2,000,000,000 may have caused it.
July 11. Temperature varied 99° to 103°; no chills; pain in feet; rather nervous but condition good.
July 18. 700,000,000 vaccines; no temperature; uneventful recovery.

The fact that is obvious from the study of these cases is that vaccines, even when sensitized, are of no value whatever in the treatment of infectious endocarditis.

The Streptococcus septicemia case was remarkable in that no focus of infection could be found. The tonsils became normal, the incision in the neck healed, but the blood culture remained positive for several weeks. There was no evidence of an endocarditis and the arthritis was obviously a metastatic process. The case was considered hopeless many times during the earlier part of the patient's illness. The interesting features of the case were: (1) almost continuously high temperature for two months; (2) failure of antistreptococcus serum; (3) huge doses of living sensitized Streptococcus hemolyticus without severe reactions; (4) final recovery, including complete recovery of function in the suppurating kneejoint.

4. SENSITIZED STAPHYLOCOCCUS AUREUS VACCINE. I have tried sensitized Staphylococcus aureus vaccine on only one case. Mr. K., suffering with furunculosis, was treated with an ordinary autogenous Staphylococcus aureus vaccine, but without permanent success.

Several months later a sensitized vaccine was prepared and a series of inoculations was given, with the result that the furuncles disappeared and have never returned.

There seems to be some evidence that in cases of Staphylococcus aureus infection, where the patient is extremely sensitive to the organism, a sensitized vaccine may be effective where the ordinary vaccine has failed. Most patients can take Staphylococcus aureus vaccine without any unpleasant results, but I have on two or three occasions encountered cases in which very small doses of Staphylococcus aureus vaccine produced constitutional symptoms and a fresh outbreak of pustules or furuncles. Under such conditions I think the sensitized vaccine is indicated.

5. SENSITIZED TUBERCULIN. I have employed sensitized tuberculin in 4 cases of tuberculous adenitis, and in 1 case of Pott's disease. Of the 4 cases of tuberculous adenitis, 2 were in children and 2 in

adults. None of the 4 cases, so far as could be told, were complicated by pulmonary tuberculosis. Three of the patients improved; 1 showed no improvement. Two of the cases which showed improvement were cases that had been operated on for tuberculous adenitis and had recurrences of tuberculous glands. Under administration of sensitized tuberculin the glands in these 2 cases disappeared. The other case which improved was a very chronic one in an adult in whom there had doubtless been considerable formation of fibrous tissue in the glands. It is not to be expected that the glands in this case would entirely disappear. The case which showed no improvement was a girl, aged seven years. She received sensitized tuberculin over a period of five months. At the end of this time the glands were fluctuating and had to be excised. The patient with Pott's disease received only two inoculations of the sensitized tuberculin. Both injections caused such marked constitutional reactions that the treatment was discontinued. The patient had extensive tuberculosis and was in no way suitable for tuberculin treatment.

Sensitized tuberculin usually excites only a mild local reaction. Exceptionally in very sensitive cases the local reaction may be quite sharp. In Case 2 I recall one severe reaction which showed itself as a large purplish-red tender nodule of the size of a walnut which persisted for two or three weeks.

The patients were all started with 0.000001 c.c. and the dosage was gradually worked up, as with ordinary tuberculin, until the dose in one case was 0.01 c.c. Sensitized bacillary emulsion appears to have no advantage over the ordinary bacillary emulsion so far as therapeutic effect is concerned, but the local reaction is somewhat less severe. As a rule the sensitized emulsion produces a mild local reaction, whereas the ordinary bacillary emulsion often gives rise to rather tender subcutaneous nodules which very slowly disappear. In some instances, however, I have seen injections of sensitized emulsion produce similar nodules.

Discussion. A great deal has been written during the past decade about vaccines, but in spite of this vaccine therapy still remains an empirical procedure. It has been repeatedly demonstrated that the injection of killed bacteria into a healthy animal calls forth the manufacture of various antibodies and that a state of immunity is thereby produced. The exact effect, however, of vaccination in the case of an infected animal or human being is not known, for the reason that no method has been worked out for studying the effect of vaccine in experimentally infected individuals. The expectations of Wright that the opsonic index would prove a reliable guide in the administration of vaccine have not been realized. At the present time the only guide is the condition of the patient. We do know that in a considerable number of cases the use of vaccine is followed by the improvement or recovery of the patient. The same may be said of sensitized vaccines. It has been maintained

by Besredka,[23] Barbat and Meyer,[24] Gay and Claypole,[25] and others that vaccination with sensitized typhoid bacilli produces a high grade of immunity, higher than that following the injection of non-sensitized bacilli. Furthermore, it has been demonstrated by Barbat and Meyer that sensitized vaccines excite a very active production of bacteriotropic bodies, while the agglutinins, bacteriolysins and complement-fixation bodies are stimulated very slightly if at all. On the other hand, the immunity attained by injections of non-sensitized typhoid bacilli is actively bacteriolytic and only slightly bacteriotropic in character. The explanation offered by Garbat and Meyer for these differences was that by means of sensitization the typhoid bacilli and their immune bodies (amboceptors) are combined so that when injected into an animal they are ready for immediate attack and destruction by the complement; whereas with the injection of non-sensitized bacteria the tissue cells must first elaborate the various antibodies before the bacteria can be sensitized (*in vivo*) and broken up. Garbat[26] suggests that if the injection of ordinary vaccine causes a bacteriolytic reaction and the administration of sensitized vaccine a bacteriotropic response it might be advisable in prophylactic vaccination to inoculate individuals with both kinds.

By this same reasoning one can account for the lesser toxicity of sensitized vaccine, on the ground that sensitization renders the bacteria more susceptible to complement, and, accordingly, more capable of rapid disintegration into harmless products. It is, of course, important that sensitization of the bacteria should be complete. In order to make certain of this an excess quantity of a serum of high titer should be used and plenty of time allowed for the firm binding of bacteria with antibody. If there is not time to immunize rabbits some of the patient's blood may be withdrawn and the vaccine sensitized with the patient's own serum.

The question whether one should use a sensitized vaccine in the living form is an important one. With the Streptococcus viridans, pneumococcus and gonococcus the living sensitized virus (in my experience) is harmless when injected subcutaneously. With the Staphylococcus aureus I should be rather afraid of furuncles in spite of the work of Broughton-Alcock. With the typhoid bacillus one should not forget the recent work of Nichols. Nichols[27] has shown that Metchnikoff and Besredka's living sensitized vaccine produces a typhoid cholecystitis when injected directly into the gall-bladder of rabbits and is therefore infectious. Furthermore, he proved that rabbits cannot be successfully immunized with this vaccine against direct gall-bladder infection.

The increased time and labor necessary for the preparation of a sensitized vaccine naturally leads one to ask the question: Is the

[23] Loc. cit.
[24] Ztschr. f. exper. Pathol. u. Therapie, 1910–11, viii, 1.
[25] Loc. cit.
[26] Medical Record, 1916, xc, 1145.
[27] Jour. Exper. Med., 1915, xxii, 780.

superiority of sensitized vaccine sufficiently marked to justify such an expenditure? In the majority of cases, no.

In the case of the typhoid bacillus the sensitized living vaccine of Besredka is infectious and is capable of producing cholecystitis in rabbits. The local reaction produced by the sensitized vaccine is slightly milder than that caused by the non-sensitized vaccine, but the difference, after all, is inconsiderable. The figures of Nichols show that in practical use on patients there is very little difference in the protective power of the two. At the present time, therefore, we are hardly justified in giving up a well-tried agent like the non-sensitized typhoid vaccine and substituting a sensitized vaccine, the efficacy of which has not yet been thoroughly established.

My therapeutic results with sensitized gonococcus vaccine were not so brilliant as to impress me with their great superiority to the non-sensitized vaccine. My limited experience with sensitized streptococcus and staphylococcus vaccine does not allow of conclusions, but I should feel about these as about the gonococcus—that if sensitized vaccine was ever indicated it would be only after ordinary vaccine had failed.

I entertain some skepticism about sensitized tuberculin. Granted that the so-called immune serum could be produced (a rather generous concession) there would probably be considerable deterioration in the imported product, no doubt several months old, when purchased in the market. Of course the latter difficulty could be overcome by substituting a domestic preparation. This same product, "S. B. E.," has been used with tolerable success by A. C. Burnham.[28] As with other forms of tuberculin the results are not so good in pulmonary as in "surgical" tuberculosis.

SUMMARY AND CONCLUSIONS. It has been shown by numerous investigators that a vaccine sensitized with an homologous serum produces less local and constitutional disturbance when injected subcutaneously than does a non-sensitized vaccine. Even living virulent organisms when properly sensitized can be injected subcutaneously without serious consequences.

It has been maintained by some that sensitized bacteria, either living or dead, produce a more rapid and efficient immunity than non-sensitized bacteria do. This question, however, cannot be considered settled as yet.

Sensitized vaccines have been extensively used for prophylactic and therapeutic purposes.

The author has employed sensitized vaccines in a series of 47 cases, which include 20 cases of prophylactic vaccination against typhoid fever, and 27 cases of therapeutic vaccination against gonococcus, streptococcus, Staphylococcus aureus and tuberculous infections. The sensitized typhoid vaccine produces a somewhat

[28] Jour. Am. Med. Assn., 1915, lxv, 146.

milder reaction than ordinary typhoid vaccine, and probably gives just as high an immunity. At the present time, however, the evidence for its superiority is not sufficient to justify the substitution of sensitized for ordinary vaccine in practice.

In the various infections treated with sensitized vaccines the results were, as a rule, no better than would have been expected with ordinary vaccine. It happened that in a few instances recovery followed the administration of sensitized vaccine after treatment with ordinary vaccine had failed. This may have been due to the fact that larger doses could be employed without untoward symptoms.

The chief objection to the general use of sensitized vaccines is the increased labor and time necessary for their preparation.

At the present time it would seem desirable to limit their use to the treatment of infections in which there is hypersensitiveness to ordinary vaccines or in which the latter have proved inefficacious.

A CHARACTER STUDY OF THE HEMIPLEGIC EPILEPTIC.

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It has been a matter of frequent inquiry whether the so-called symptomatic or organic epileptic possesses the epileptic make-up or constitution,[1] and whether the mental stigma of his disease has any of the defects in primary instincts which are usually so obvious in idiopathic or essential epilepsy. While a study of the hemiplegic epileptic based upon infantile cerebral palsy and its attendant epilepsy cannot be considered as a strict criterion of the adult or organic group of epileptics, a study of such material may be considered as an earnest to the right approach to this symptomatic group of epileptics.

Several years ago Dr. Sharp and I undertook a study of the inheritance and presence of neurotic stigma in the families of the hemiplegic epileptics at the Craig Colony;[2] 433 cases of hemiplegic epilepsy were considered. We concluded that "the heredity factor in hemiplegic epilepsy is only a little less in evidence than that present in genuine epilepsy, and that the prognosis as to a sequential epilepsy following in the wake of a given case of infantile cerebral

[1] Clark: A Personality Study of the Epileptic Constitution, Am. Jour. Med. Sc., 1914, cxlviii; see also Clinical Studies in Epilepsy, Psychiat. Bull., January, 1916 to January, 1917.

[2] Clark and Sharp: The Role which Heredity Plays in Inducing Epilepsy in Children Suffering from Infantile Cerebral Palsy, Jour. Nerv. and Ment. Dis., 1913, xl, 633.

palsy should be based upon the presence and degree of spasmophilia or neurotic history in any given case, and that this latter fact should be given as much or even more weight than the site, nature and degree of the initial cerebral injury expressed in the palsy."

In the foregoing statement as to the heredity factor in hemiplegic epilepsy, that the heredity in its frequency and degree runs almost if not quite parallel to that of essential epilepsy, it becomes doubly important for us to study the essential make-up of such individuals before the onset of their palsy as well as the symptomatic sequela of epileptiform attacks. To this end I have made a careful study of the make-up of a selected group of hemiplegic epileptics who are now, so far as their mental state is concerned, quite identical to those suffering solely from essential epilepsy.

The data summarized here are from 12 cases of hemiplegic epilepsy. The epileptic character was found in one side of the fraternity most frequently. Occasionally a high volatile explosive temper, combined with an intense egotistic self-centered and sensitive make-up, was present in both sides of the fraternity. From this actual small data the paternal parent was found invariably to be quick-tempered, while the mother and her family stock were usually mild and docile. In the whole material there were but 2 cases in which some marked degree of the epileptic make-up could not be found in the patient several years before the advent of the palsy or even from birth. The epilepsy seemed but a natural corollary made mandatory by the presence of a cerebral palsy in such children. Often enough several other children in the same family showed some degree of the same character. It would seem, however, that these siblings escaped epileptic reactions largely if not solely because their keen egotistic tendencies became fairly easily subordinated, or they socialized them, as most frequently obtains in other passionate-tempered and difficult children during early adolescence. Mental and physical characteristics similar to the hemiplegic epileptic were also possessed by the siblings of the same family, and in a few instances they continued to possess this type of make-up and had continued passionate outbursts of temper but no well-defined epileptic seizures occurred.

In brief, it may be said that (1) the hemiplegic epileptic has about the same neurotic inheritance as the essential epileptic; (2) he has also about the same degree of epileptic constitution before the onset of his palsy.

After the more or less certain advent of his epileptiform seizures the hemiplegic epileptic deteriorates physically and mentally more certainly and rapidly than his essential epileptic fellow. I have never known a hemiplegic epileptic to recover from his epilepsy, although in a few instances they have been immune from epileptic attacks for months, and in one instance of my own for more than a year. He is best conserved from rapid mental deterioration by a well-directed effort to maintain a proper mental hygiene and as wide and

intensive a field of interest as possible for one who has a paralytic handicap which is an added integral debit to his natural temperamental disability.

We have under study 12 hemiplegic epileptics between the ages of nineteen and thirty-five years, divided equally between the two sexes, all at present under institutional care.[3]

The majority of these patients (9) belonged to large families ranging all the way from three to nine members; one patient was an only child. In 5 cases they were the first born; in the others they were born between other children who were healthy and strong.

In 6 cases the father was dead, 3 of whom were described as having been "moderate drinkers." Two of the latter died of paralysis and Bright's disease. Other causes of death in the paternal parent were: progressive paralysis due to abscess; pneumonia; arteriosclerosis. In 1 case the mother was alcoholic and died of Bright's disease. Another died of mastoiditis. The other 8 were living and claimed to be healthy, with the exception of 1, who is now suffering from a form of insanity which did not develop until our epileptic patient was fifteen years old.

All of the patients under study were of normal birth, no instruments used, and were breast fed. Only 1 suffered from constipation as a baby. For the most part they were not very passionate as infants and were easily managed, with the exception of 3, who are described as crying and irritable.

The hemiplegia came on in one case after measles at eighteen months. In a second after diphtheria at three years; in a third and fourth after no sufficient cause at sixteen months and two years respectively; in a fifth after pneumonia at one and one-half years; in a sixth after a slight fall at twenty months; in a seventh after scarlet fever at six years; in an eighth after an attack of apoplexy at twenty-five years of age. In 3 cases the hemiplegia appeared to have been noticed on learning to walk, about the second year. In one case the hemiplegia came on at ten and one-half years, with no apparent cause; this latter patient's skull was opened and nothing abnormal was found.

In 8 cases the paralysis involved the entire right side and incapacitated the patient to a greater or less degree. In 1 case the right hand only was involved. Three cases showed a left hemiplegia. It is interesting to note in one of the latter cases the patient showed the typical epileptic constitution as shown in a study of the idio-

[3] In order to make this clinical study as accurate as possible, the same general precautions in collecting data were observed as those in my study of the personality of the essential epileptic. In addition, through the kindness of Dr. William T. Shanahan, superintendent of Craig Colony, to whom my best thanks are due, the case material was taken from that institution, and all were drawn from those admitted to Craig Colony from the New York City district. In this way I was able to gain as many interviews from relatives as were found necessary to make me sure of the data thus collected.

pathic epilepsies, but the epilepsy itself did not appear until her twenty-third year.

All were bright up to the time of the occurrence of the hemiplegia, and in some instances for many years after.

Probably due to a lack of observation on the part of the parents no petit mal attacks seem to have been noted before the onset of the grand mal epilepsy. In 2 cases only was there any record of there having been "dizzy turns" antedating grand mal attacks.

There are three distinct periods in which the onset of the grand mal epilepsy has a tendency to group itself in the cases under study; in very early childhood from eighteen months to three and one-half years; around adolescence from eleven to fourteen years; in 2 cases as late as the twenty-third and twenty-fifth year.

The descriptions given of the aura are for the most part very hazy. In 1 case there was "pain in the stomach;" another felt a numb sensation in the hand and felt very nervous five minutes before the attack; a third "felt irritable;" a fourth felt "dizzy;" another stated he felt "disturbed;" two others "felt the attack coming on" and called for assistance.

As stated all 12 cases are under institutional care and have been for several years. It is interesting to note that a half show little deterioration as yet. A few even show improvement, and these individuals are the ones who appear to enjoy colony life and have no inclination to return home, in most instances finding much more to keep them healthfully employed and interested there than in their former surroundings. The other half are gradually deteriorating mentally and physically; they are slower, their memory is becoming poorer and they show dissatisfaction and a lack of interest in their environment, and continually write to be allowed to return home.

A picture of the personality of the hemiplegic epileptic may be made up as follows, each characteristic having been considered separately and found to hold true in the majority of the cases studied.

The standing in school was, on the whole, rather poor; they were slow to grasp facts. They were quick and impulsive. Power of concentration and observation was fair. They showed good common sense and were self-reliant. There was almost a total lack of imagination and originality shown in play. There was only a slight tendency toward bashfulness and shyness. For the most part they were neat, clean and orderly, but not especially committed to routine. They played freely with other children, but as many showed a tendency to be domineering, they were not favorites among their playmates. They showed a tendency to be stubborn and difficult to handle before the onset of their epilepsy, and these characteristics became more marked after the epilepsy was in evidence. The majority were trustful and not suspicious, but nearly all were keenly sensitive, easily offended and saw slights when none were intended. A few patients showed a tendency to hold grudges. For

the most part there was a tendency for the hemiplegic epileptic to become more keyed up and irritable just before attacks, and after the attack had passed things would run smoothly for several days until "things began to pile up again."

There was a tendency toward assuming a pietistic attitude, but there was a lack of sincere religious zeal. They were frank and open toward the parents in a superficial degree. Half of the group under study were demonstrative and affectionate toward members of the family, while the other half showed a total lack of this trait.

Apparently, from the records, there were no exhibitions of tantrums before the epilepsy developed, a trait often seen before the advent of attacks in the idiopathic epilepsies.

They were neither overcourageous nor cowardly. Some were given to anxiousness and forebodings. As a rule they were truthful. A few were fantastic, but the majority were very matter-of-fact in their attitude toward life. There seemed to be little tendency to day-dreaming and castle-building, so far as the relatives were able to state. The general mood for the most part was one of over-seriousness, yet a few are depicted as being cheerful, happy and good-natured.

The hemiplegic epileptic has a very shallow grasp on anything in the intellectual field, and therefore likes to busy himself with various light duties, running errands, pulling weeds and various kinds of house and garden work, but they are incapacitated by their paralysis from doing manual labor in an efficient manner and show little ability to do anything well.

There have been various bereavements experienced by the patients studied, but only 2 have reacted keenly to the loss of a parent or near relative; for the most part there has been no deep reaction and little tendency to crave sympathy.

On the whole the mood is stable. There is a tendency to show more irritability and quick temper as the epilepsy advanced.

As a general rule the mother of the hemiplegic epileptic was found to be of the docile type, while the father was quick-tempered and easily aroused. Of the few cases recorded to resemble in physical or mental make-up one of the parents, there was a tendency to take after that parent who showed the liveliest temper.

Several of the group showed a desire to lead, but their playmates did not readily accede to their demand, and hence there were quarrels and feelings of jealous rage were engendered in the epileptic. Others of the group showed no tendency to dominate. A few liked to moralize and held others up to criticism, but did not care to be criticized themselves and had a tendency to blame others for their own shortcomings. They were fond of eating.

Unfortunately there seemed to be nothing in his environment from which the hemiplegic epileptic derived deep satisfaction. One liked to draw pictures, another liked to walk, a third was fond of

being well dressed; but aside from a very superficial interest in various things there was nothing from which they derived a soul satisfaction. In half of our group study, as the years passed, there was a tendency to deteriorate physically and mentally; the mind dwelled in the past while the memory content for recent events was hazy. The other half of our group managed to keep alive an interest in their colony existence and were able to inject themselves into their environment, and these are the type of individuals who showed less tendency to deteriorate; the onward march of the disease seemed to be held in abeyance, while one or two are said to even show improvement.

In conclusion one may say that epileptiform attacks following in the wake of infantile cerebral palsy are not dissimilar in their final results to those of a frank and enduring essential epilepsy. They have about the same degree of heredity as their idiopathic cogener, and there is present about the same degree of personality make-up in the individual who suffers from it. A more extensive study along the same general lines should be made, and, finally, the same painstaking investigation ought to be made upon epileptics who are supposedly made so by other cerebral insults of adult life. There are reasons, as well as some data already collected, to show that this latter material will disclose not dissimilar results to those shown in this small study of infantile cerebral hemiplegic epilepsy.

STUDIES IN FRACTIONAL ESTIMATION OF GASTRIC CONTENTS. II. EFFECTS OF ANTACID MEDICATION ON GASTRIC ACIDITY AND SECRETION.[1]

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The effect of antacid medication, particularly the alkaline salts, upon the human and the animal stomach is still a matter of dispute. The general impression of those who are not familiar with this issue is that the alkali acts as a specific antagonist to the acid secretion of the stomach, neutralizing the acid and thus satisfactorily reducing the hyperacidity. This was the empirical basis upon which, for

[1] This study was accomplished under the tenure of a George Blumenthal, Jr., Fellowship in Pathology.

many years before the birth of the present-day experimental medicine, the antacid qualities of the mineral springs of Vichy, Ems, Carlsbad and other resorts were so warmly recommended by the profession as a cure in gastric disorders of the hyperacid type. Jaworski,[2] an enthusiastic defender of the efficacy of the Carlsbad waters, stated, in 1888, that the alkaline properties of these waters caused an atrophy of the secreting tubules and converted hyperchlorhydria into hypochlorhydria. This effect was supposed to be carried to the point of setting up a gastric catarrh, associated with a diminution of the acid supply. Much apparent support was lent to this view by the experimental work of Pawlow,[3] Bickel,[4] Heinsheimer,[5] Rosenblatt[6] and others. As an example of the best type of experiment upon which such a view was founded one needs but read the results of Pawlow. A dog with multiple fistulæ was fed meat saturated with bicarbonate of soda. As a result Pawlow[7] noted a diminution of all the alimentary secretions, gastric, salivary, pancreatic and intestinal, and a definite delay in the emptying time of the stomach.

However the doctrine of the inhibitory action of the alkalies on acid production was not to go unchallenged; an immediate protest was noted on the part of the clinicians. They attempted to control, by repeated test meals on patients suffering from hyperchlorhydria, the animal experiments as carried out in the laboratory. The contradiction of the laboratory findings by the bedside conclusions of the clinicians was striking. Du Mesnil,[8] feeding to a patient increasing doses of alkali (soda bicarbonate), found, as a result, on successive days an increasing daily acidity. Von Leube[9] held that bicarbonate of soda, although neutralizing temporarily, gave rise to a secondary stimulation of the acid secretory glands. The most striking refutation was offered by Linoissier and Lemoine,[10] who utilized a subject of merycism for repeated experiments to establish the therapeutic efficacy of bicarbonate of soda. Their results are given in the following words: "The immediate effects of bicarbonate of soda on gastric secretion are excitant whatever the dose. The first effect of the excitation is to saturate or neutralize the acidity if the dose is weak or moderate; an augmentation of the chyme and hydrochloric acid is produced. If the dose is massive, neutralization is attained, following which an arrest of hydrochloric acid production may occur, but before the normal acidity

[2] Wien. med. Presse, 1888, xxix, 87.
[3] The Work of the Digestive Glands, 1910.
[4] Berl. klin. Wchnschr., 1905, xliii, 869.
[5] Med. Klin., 1906, ii, 616.
[6] Inaug. Dissert., Berlin (quoted from Boas: Diag. und Therap. der Magenkrankheit, sixth edition, 1912, p. 351).
[7] The Work of the Digestive Glands, 1910, p. 232.
[8] Deutsch. med. Wchnschr., 1892, xviii, 1112.
[9] Ziemssen's Handbuch Therap., 1874, vii, 220.
[10] Bull. gén. de therap., 1894, cxxvii, 492.

is reached the food may have left the stomach." Further, they saw at Vichy an anacidity case converted into one of hyperacidity by drinking of the alkaline waters of the spring. Bourget,[11] by careful observations in his clinic, using the method of successive test meals, was fully convinced that the alkalies caused an eventual augmentation rather than diminution of gastric acidity.

And yet the issue between the research workers in the laboratory and the clinicians was not clear cut; contradictory testimony to both views was not lacking. Claude Bernard,[12] the distinguished physiologist, distinctly stated as early as 1879: "En faite, on sait tres bien que le suc gastrique s'ecoule en plus grande abondance quand on introduit des alcalines dans l'estomac; les acides au contraire, entrarent sa formation."[13] Mathieu and Laboulais,[14] using the repeated test-meal method on human subjects, found conclusions contrary to those of the body of clinicians, observing a diminution of hydrochloric acid production both after immediate alkali administration and after the prolonged use of alkalies therapeutically.

The standard modern text-books on pharmacology and therapeutics reflect the views of these two opposing schools of observers, without adding any testimony which would tip the scale in favor of either one.

Personal Experiments. In a previous paper it was suggested that the method of fractional estimation of stomach contents offered many new facts regarding the course of human digestion and the cycle of chemical activity. The method lends itself as a means toward the further investigation of the action of drugs and diet upon the secretion of the stomach. Introduced by Schuele[15] and Ehrenreich,[16] and recently elaborated and extended by Rehfuss,[17] the fractional test is an ideal one for further experimentation on such a subject. By allowing of the withdrawal of specimens of chyme at short intervals throughout the duration of digestion it offers the opportunity of charting the variations in the secretion of acid and ferments, also of observing the emptying time of the organ. Further, one is enabled to note the effect of drugs on the reflex flow of duodenal contents and of the secretion of gastric mucus.

The method employed in the following experiments is identical with that used in the previous publication. In the former paper[18] the deviation from the normal of the various factors incident to disease was ascertained and studied. The experiments in this

[11] Die Krankheiten des Magens und Ihre Behandlung, 1906, p. 90.

[12] Leçons de phys. oper., 1879, p. 570.

[13] "Actually, one notes an abundant secretion of gastric juice upon the introduction of alkalies into the stomach; acids on the contrary arrest its production."

[14] Bull. et mém. Soc. méd. d. hôp. de Paris, 1894, xi, 615.

[15] Ztschr. f. klin. Med., 1895, xxviii, 461.

[16] Ibid., 1912, lxxv, 231.

[17] Am. Jour. Med. Sc., 1914, lxiii, 11.

[18] Crohn and Reiss: Am. Jour. Med. Sc., 1917, cliv, 857.

study were performed on the emptied fasting stomach in the morning. A heavy oatmeal gruel was utilized as the test meal. Specimens of chyme were withdrawn every fifteen minutes until the viscus was again empty, as evidenced by the failure to obtain further specimens. The motility of the organ was adjudged by noting the last specimen to give the starch reaction with iodin. The regurgitation of bile was carefully observed, as was also the presence of the heavy, ropy mucus characteristic of the pyloric mucous secretion. In every case, on one or more days previous to the experiment, a control curve without medication was plotted.

The patients upon whom the experiments were made were all cases of mild functional disturbances; individuals with definite organic lesions were not included. The majority of the experiments were performed on patients with isosecretory or hypersecretory types of curve except when otherwise stated in the text. Illustrative single examples are described in the paper; each individual experiment was, however, sufficiently controlled by frequent repetitions, often on different patients.

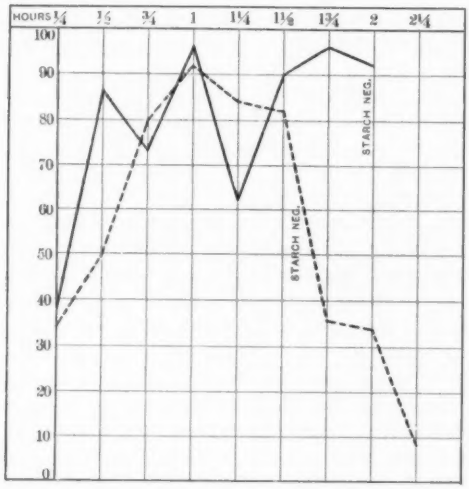


FIG. 1

EFFECT OF ALKALIES ADMINISTERED TO THE FASTING STOMACH BEFORE A MEAL. Magnesium oxide (calcined magnesia) was employed in this experiment and was administered in 1-gram dose one-half hour before the test breakfast. The effect was at once apparent (Fig. 1). An acid curve which reached its height (94 per cent.) at the end of one hour and then gradually fell to zero, was converted into a curve in which the maximum height (86 to 96 per cent.) was achieved at the end of the first half-hour

and was maintained practically constant at this level to the end of digestion. In other words a mild hyperchlorhydria existing for three-quarters of an hour during the height of digestion was converted into a hyperchlorhydria of greater degree and maintained as a constant for one and three-quarter hours. Numerically expressed, an average total acidity of 55.6 per cent. had been converted into an average total acidity of 78 per cent. In the control experiment the stomach was free of starch one and a half hours after the introduction of the test breakfast; after the administration of the magnesia the final emptying was delayed to two hours after eating. In the control experiment a beneficent regurgitation of bile marked the decline of the acid curve; in the instance with magnesia this was not observed.

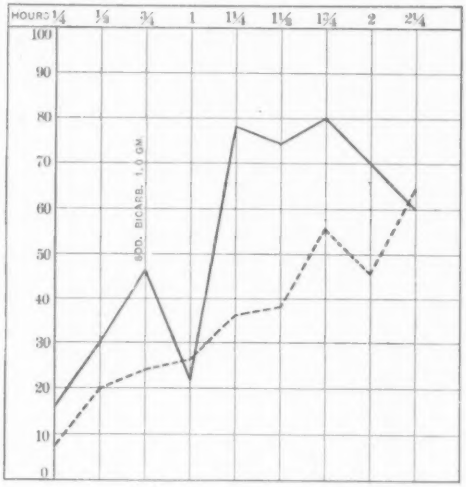


FIG. 2

EFFECT OF ADMINISTRATION OF ALKALIES IN SINGLE DOSE DURING DIGESTION. Bicarbonate of soda in 2-gram dose (30 grains) was given to a patient three-quarters of an hour after the onset of digestion. In fifteen minutes the acidity dropped from 46 to 22 per cent.; within another fifteen minutes it had rebounded to 78 per cent., which level it maintained for one-half hour and then slowly declined (Fig. 2). Numerically expressed, an average acidity of 43.6 per cent. in the control test was converted into an average acidity of 64 per cent. upon the administration of 2 grams of bicarbonate of soda. The total depression of acidity following the taking of the salt was for the duration of one period only, or fifteen minutes; the secondary augmentation of acid was for the

duration of the entire remaining portion of the digestive cycle. No delay in motility was noted in this instance.

On administering to another patient twice this dose of bicarbonate of soda (4 grams—60 grains) the reaction of the stomach to the alkali was so rapid that the very first specimen of chyme withdrawn fifteen minutes after the exhibition of the bicarbonate showed an increase in the acid titer. This demonstration of the evanescent action of sodium bicarbonate is occasionally confirmed by the personal experience of those who have employed this salt for the relief of heartburn or hyperacidity.

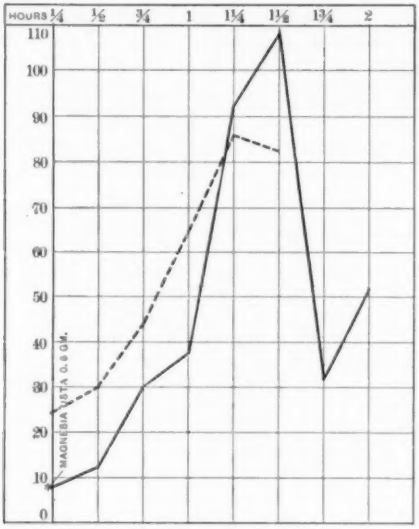


FIG. 3

Magnesium oxide (calcined magnesia) was chosen as the type of more slowly acting, but more efficient alkali. In an experiment in which it was administered directly after eating, in dose of 0.3 gram (4.5 gr.), it caused a negligible diminution of acidity (34.6 to 32.2 per cent.). The emptying time of the stomach was, however, delayed; in the control test it was one and three-quarter hours, in the test after medication it was two and a half hours. The delay in motility was attributable to the rise in acidity late in the course of digestion. As in the previous experiment with bicarbonate, one noted the absence of the bile which normally regurgitate as the acidity falls toward the end of the secretory activity.

Upon doubling the dose of the magnesia (0.6 gram or 9 grains) to another patient the average total acidity was decreased from

54.6 per cent. without medication to 46.5 per cent. after the magnesia, but the curve of acid secretion was completely disfigured. Following the administration of the alkali a maximum acidity of 86 per cent. in the control test was converted into a hyperacidity of 108 per cent., thus again affording an illustration of the unfavorable reaction of the gastric mucosa to the presence of alkalies. The resultant curve is illustrated in Fig. 3. The motility was slightly delayed.

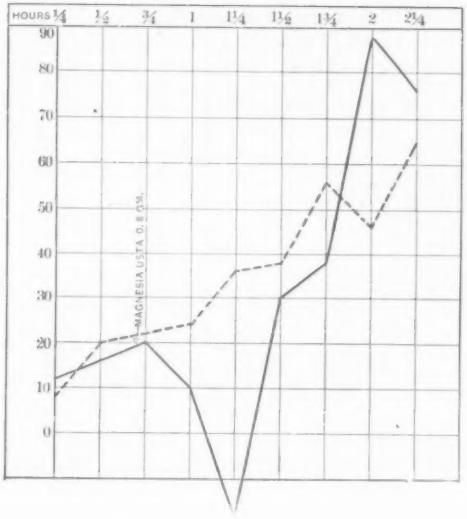


FIG. 4

To a third patient magnesium oxide 0.8 gram (12 grains) was given. The drop in acidity was less rapid but more prolonged and of greater magnitude than in the bicarbonate series. Thus in the first fifteen minutes after the medication the acid titer fell from 20 to 10 per cent.; in the next period it fell from 10 per cent. acid titer to 5 per cent. alkaline titer, a total fall of 15 per cent.; however, in the course of the next three periods or forty-five minutes an irritative reaction on the part of the stomach was observed. The acid titer rose rapidly to 26 per cent., then to 38 per cent. and finally to 88 per cent., exceeding at this point the maximum acidity in the control test by 24 per cent. (Fig. 4). It was evident that what had been gained by the initial neutralization was more than compensated for by the subsequent increase in acidity. The average total acidity was decreased from 40.6 to 34.6 per cent.

EFFECT OF ADMINISTRATION OF ALKALI AT END OF TEST MEAL. A dose of magnesium oxide, 0.8 gram (12 grains), given one and three-quarter hours after the ingestion of the test gruel, caused a rapid and efficient neutralization of the digestive acidity without secondary rise (Fig. 5).

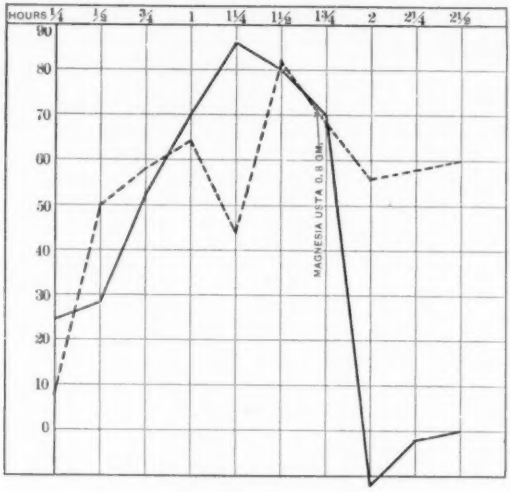


FIG. 5

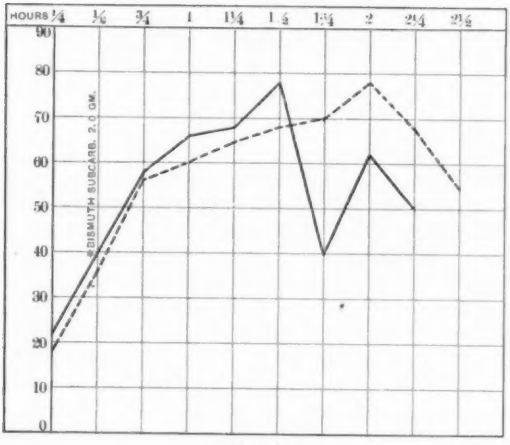


FIG. 6

ANTACID EFFECT OF BISMUTH SUBCARBONATE. The resultant curve, occurring from the administration of bismuth subcarbonate

in 2-gram dose directly after the meal, was obtained. A diminution of acidity was observed to take place without a corresponding compensatory increase in the acid secreted. The total depression of the acid was almost 50 per cent.; a very slight prolongation of motility was observed. The neutralizing action of the bismuth salt was efficient, moderate and prolonged and without deleterious after-result. In a duplicate experiment on another patient using a slightly greater dose the acidity was depressed from 56.8 to 45.2 per cent., without delay in motility or secondary reaction (Fig. 6).

KAOLIN: ACTION OF AN INERT MINERAL EARTH ON GASTRIC ACIDITY. This substance was chosen in an attempt to estimate the adsorbent power of an inactive mineral matter. No effect was apparent.

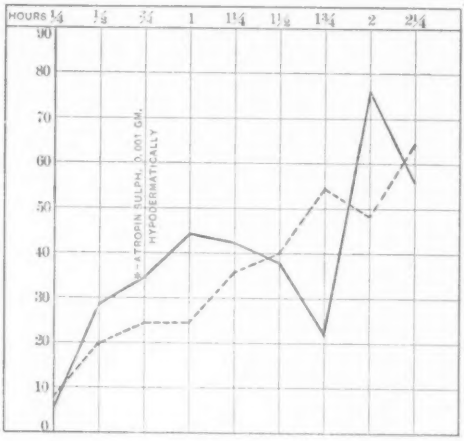


FIG. 7

ATROPIN: ITS EFFECT ON GASTRIC SECRETION AND MOTILITY. A patient whose control curve had been previously ascertained was given 1 mg. of atropin ($\frac{1}{60}$ grain) hypodermically three-quarters of an hour after the ingestion of the test gruel. Little or no result was seen, except that in the last half-hour there was a rapid rise of acid from 32 per cent. to a maximum of 76 per cent. No diminution of acidity was observable at any time; in fact, there was a slight rise of average total acidity (35 to 38.6 per cent.) (Fig. 7). Motility was unaffected. A similar experiment in another patient gave practically identical results.

In the hope of obtaining a better result by the prolonged administration of this alkaloid the former patient was fully atropinized by the taking of moderate doses of atropin by mouth for several days. A fractional estimation made at this time failed to exhibit

the slightest variation from the control curve (Fig. 8). The average acidity had increased rather than diminished, namely, from 35 to 51.1 per cent. Motility was unaffected. The patient was showing at the time of the experiment the signs of early belladonna poisoning, that is, dilated pupils, dry mouth, etc.

ATROPIN: ITS EFFECT ON CASES OF HYPERSECRETION. The previous experiments were performed upon patients with isosecretory curves or on those showing only slight hyperacidity. The pharmacological action of belladonna is that of diminishing secretion. It was therefore of interest to observe the effect of the atropin in cases of hypersecretion both as regards the effect upon the acidity as well as upon the secretion of the watery, gastric juice characteristic of the disease. The following conclusions are based upon experiments with two cases of hypersecretion:

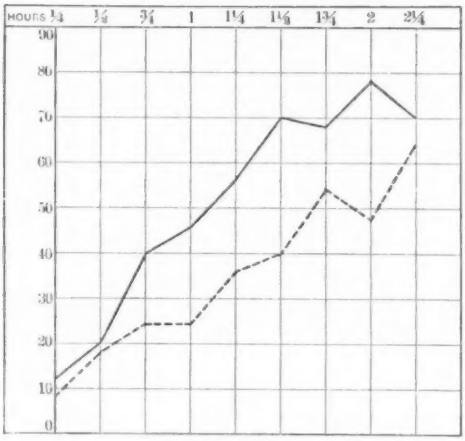
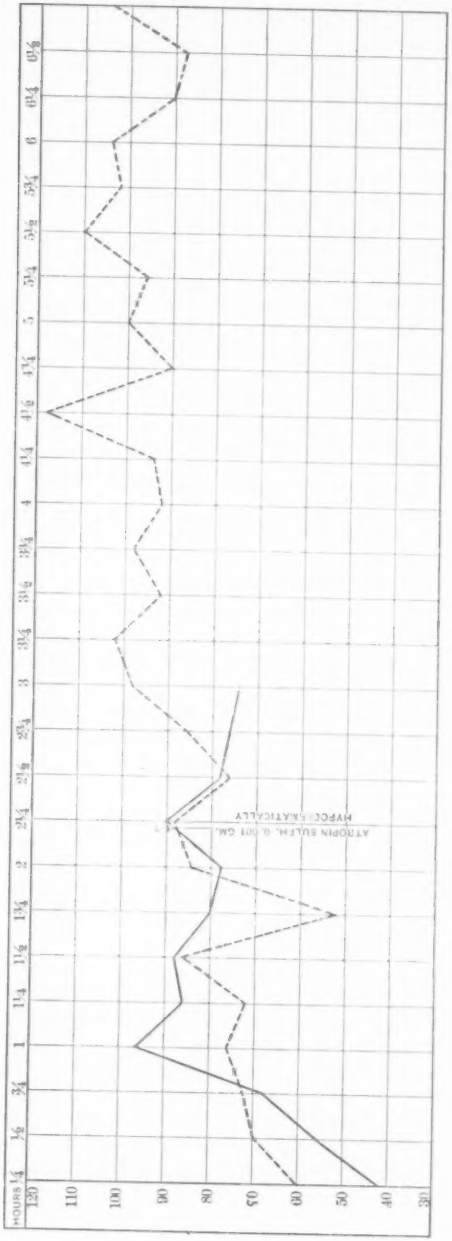


FIG. 8

The first case was one of functional hypersecretion of the continuous type, so-called Reichmann's disease. An exploratory laparotomy had failed to show any organic lesion. Upon administering the usual gruel test meal a highly acid gastric juice was secreted which continued as long as observed (six and three-quarter hours). All food had left the stomach after two and three-quarter hours, and yet the secretion continued. An average total acidity of 89 per cent. was estimated. The test was repeated on a succeeding day; after two and one-quarter hours the stomach became free of the last traces of the oatmeal gruel; the hypersecretion continued. At this point the patient was given by hypodermic 1 mg. of atropin ($\frac{1}{60}$ grain). Within an hour the secretion had


HOURS
120
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80
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30
½
¾
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5
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5¾
6
6¼
6½
ATROPIN SULFH. 0.001 GM.
HYPODERMATICALLY

FIG. 9

ceased, the total acid titer diminishing gradually to 56 per cent. The patient was thereupon fully atropinized by being put on atropin sulphate by mouth in large doses for three days. A fractional test made at this point showed a delay in motility to three hours, but the secretion ceased three and one-half hours after taking the test meal. The average total acidity was reduced to 60 per cent. (control, 89 per cent.).

In the second case of continuous hypersecretion the secretion of acid juice lasted five and one-half hours or more after the ingestion of the test meal; the average total acidity was 85.3 per cent.; emptying time was three and one-half hours. On a subsequent day atropin sulphate 0.0012 gram ($\frac{1}{50}$ grain) was injected hypodermically one-half hour before the test meal was given. The effect was very striking. Secretion ceased after two and one-quarter hours; acidity was reduced to an average total acidity of 47.3 per cent. Motility was improved, the stomach emptying in two and three-quarter hours.

While the result in this case of atropin administered hypodermically before the meal was very effective in reducing both the hypersecretion and the hyperacidity, yet it was recognized that for continuous usage such a method was not practical. Therefore after an interval of a few days the experiment was repeated, except that the atropin in identical dose was administered per oram. The result was disappointing, the hypersecretion continuing for seven hours and the average total acidity being raised from 85.3 per cent. in the control to 90.4 per cent. in this test. The motility was unaffected.

The patient was now given 1 c.c. of tincture of belladonna four times a day, this being continued for three days until the physiological results of the drug began to manifest themselves. A fractional test made at this time showed an increase of average total acidity from 85.3 to 104.5 per cent., but a diminution of the duration of the hypersecretion, the latter ceasing after three hours.

Olive Oil: Does it Affect Gastric Acidity? Two ounces of olive oil were administered to a patient whose control curve had previously been ascertained. The resultant figures were disappointing in that a slight rise rather than a fall of total acidity resulted, namely, from 35 to 40.6 per cent. The motility of the stomach was unaffected, the organ emptying itself identically in both instances, *i. e.*, in two and one-quarter hours (Fig. 10).

In a case of continuous hypersecretion a better effect was observed after the use of olive oil. One-half hour after the fractional test was begun 90 c.c. of olive oil were administered. The average total acidity was reduced from 101.5 to 81.6 per cent. on one occasion and from 94.5 to 87.6 per cent. on another occasion. The factor of hypersecretion was affected to a lesser degree.

ADMINISTRATION OF ALKALIES IN DIVIDED DOSES DURING DIGESTION. The previous observations of the effects of the alkaline earths on the gastric acidity demonstrated two phases of activity,

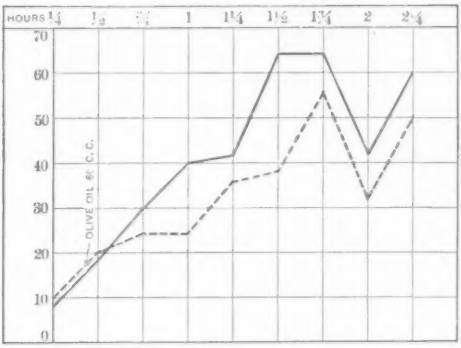

FIG. 10

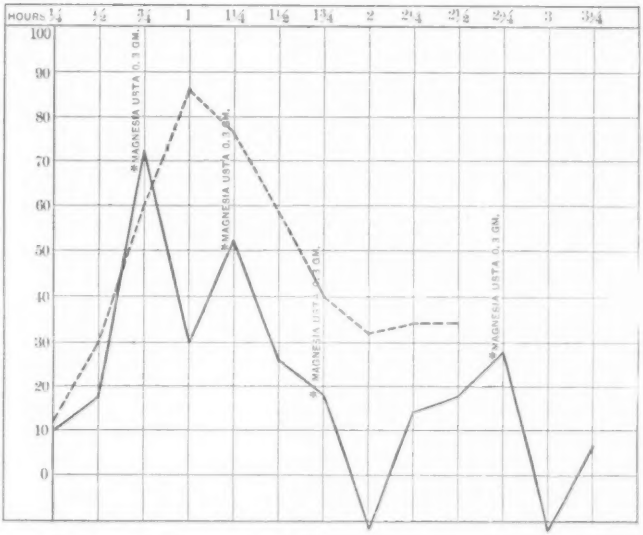

FIG. 11

a primary neutralization phase and a secondary or compensatory reaction marked by excessive acid production. The attempt was made to cause a continuous depression of the acid curve by dividing the single dose of alkali into aliquot portions and distributing these

portions over the course of the digestion. Calcined magnesia was chosen as the alkali to be tested, since the nature of its therapeutic activity had been previously ascertained. Thus after a single dose of magnesia (20 grains) it had been learned that the primary or depressant stage lasted about thirty minutes and was followed rapidly by a sharp rise in the acidity. A fractional dose of the magnesia (5 grains) was therefore administered every half-hour for four doses. The effect is charted in Fig. 11. A successful depression of the acid curve was accomplished, the neutralization of the acidity being both complete and permanent. In fact, the successive doses had an apparently cumulative action, so that after the third dose an alkaline reaction in the stomach contents was actually observed. The diminution of average total acidity was from 43 to 22.4 per cent.

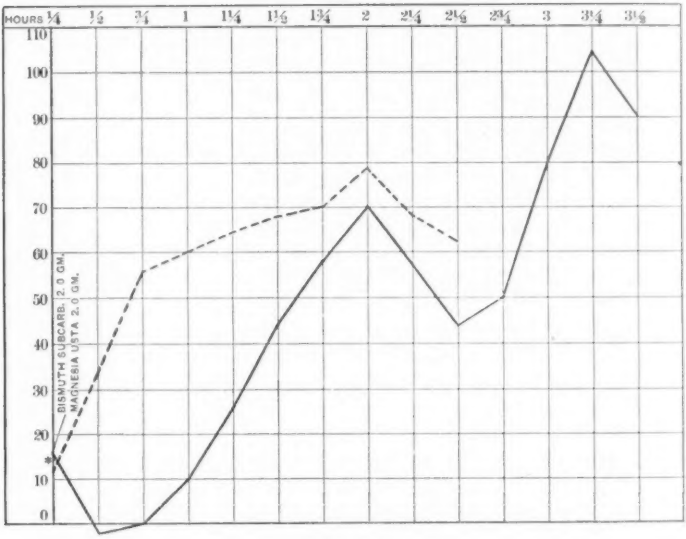

FIG. 12

EFFECT OF ADMINISTRATION OF COMPOUND MEDICATION. The therapeutic action of antacid agents in combination, was investigated by the administration of a compound powder after the ingestion of the test meal. The first combination investigated was: ℞—Magnesiæ ustæ, gr. xxx; bismuth. subcarbon., gr. xxx. The resulting curve showed the predominance of the action of the magnesia. Following the taking of the powder there was a rapid neutralization of acidity to minus 4 per cent. (4 per cent. alkalinity), followed by a progressive rise to 104 per cent. total acidity. Free

acid was completely absent for one hour; motility was delayed to three and three-quarter hours (control time two and one-half hours). The average total acidity was unappreciably reduced from 56.8 to 48.8 per cent. The curve was divided into two phases: In the first an exaggerated and unphysiological depression took place and in the second just as unphysiological an hyperacidity was created. The magnesia effect was the predominant one, the deliberate and steady antacid qualities of the bismuth being unobservable. It was evident that the dose of magnesia had been too large.

A second combination powder of the following composition was administered: ℞—Magnesiæ ustæ, gr. xv; bismuth. subcarbon., gr. xv; sodii bicarbon., gr. xx; atropinæ, gr. $\frac{1}{100}$.

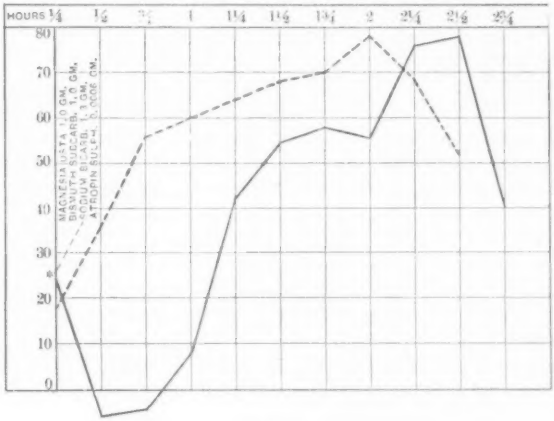

FIG. 13

A more moderate effect was here observed (see Fig. 13). The initial depression was too rapid and was carried too far because of the presence of the bicarbonate of soda; however, the secondary rise of acidity was also less marked because of the smaller dose of magnesia employed. The depression of average total acidity was from 58.6 to 38.7 per cent.; motility was not delayed. The late and more even action of the bismuth was more in evidence in this test.

As an example of the vicious use of an overdose of antacid agents the action of the following combination powder is cited: ℞—Magnesiæ ustæ, gr. xxx; bismuth. subcarbon., gr. xxx; sodii bicarbon., gr. xxxx.

An excessive, early and prolonged neutralization of the acidity was observed. An actual alkalinity of 70 per cent. occurred within fifteen minutes after the administration of the powder.

Free acid was absent for two hours, following which there was a return of the total acidity to 68 per cent. The diminution of the average total acidity was very marked, namely, from 58.8 to 13 per cent. It is self-evident that such an extreme depression was contrary to the physiological conditions for digestive activity, and was probably as deleterious, if often repeated, as the uninterrupted hyperchlorhydria would have been.

Discussion of Results. The preceding experiments portrayed in an exact and concrete manner the method of action of the various agents commonly employed by the medical profession to encompass a diminution of the acidity of the stomach and of its secretion. The customary alkalies, sodium carbonate and calcined magnesia, were carefully studied, as were also bismuth subcarbonate, olive oil and atropin; the latter are constantly being empirically used for the attempted accomplishment of the same aim.

As regards the alkaline salts, both the soda and the magnesia act therapeutically in a relatively similar manner. Both neutralize the acidity at the moment of administration, the bicarbonate more quickly but less thoroughly, the magnesia more slowly but more effectively. The administration of either salt is followed by an irritative reaction in which the acid mounts quickly, to at least the level of the control test at the corresponding time. In most instances, particularly with the magnesia, the secondary rise in acid exceeds all previous levels. While it was true that the average total acidity may have been depressed when a sufficiently large dose was employed, yet this figure for acid diminution should be accepted with reserve, for it often gives a fallacious impression. Thus an immediate depression of acidity to minus 70 per cent. (70 per cent. alkalinity) may be counter-balanced by a secondary rise of acid titer to plus 110 per cent.; in such an instance the general average may be well within the normal figure and evidence no variation from the control average acidity. It now becomes apparent why such divergent results were obtained by Bourget,[11] Hayem,[19] Du Mesnil,[8] Lenoissier and Lemoine[10] and others, for each investigator chose a different time after the administration of the alkali at which to extract his test meal.

The interpretation of the charts of fractional estimations, throws a most illuminating light upon the mode of action of these salts as commonly employed. The custom of administering alkalies before meals, as is practised by some of the medical profession, is a mistake, for the reason that the meal comes at the time of the secondary reaction to the alkali and thus the digestive acidity is reënforced rather than diminished. The administration of these salts after the meal was attended by better results when the proper dose was chosen. Thirty grains of bicarbonate of soda produced no depres-

[19] Hayem: Lecons de Therapeutique, les Agents Physique et naturels, p. 609.

sion, in fact produced a rise in average total acidity, and yet the temporary neutralization was moderate and physiological and the secondary rise not exorbitant. Sixty grains caused a general depression, yet by generating a secondary medicinal hyperacidity defeated its own purpose. All in all the former dose was preferable at least for a case of moderate hyperacidity; a hyperchlorhydria which reaches 90 per cent. and over probably requires a proportionate increase in dosage.

The disadvantages of a large dose of magnesia, 15 grains or more, are: (1) That the initial depression is excessive, robbing the stomach of its essential free acid for a period varying from half an hour to two hours; during this period proteolysis is paralyzed, since free acid is essential to the digestion of proteid. (2) The subsequent reaction on the part of the acid-secretory cells is so vigorous that the therapeutic purpose is defeated. The dose of magnesia should therefore be a moderate one, 8 to 15 grains, depending on the degree of hyperchlorhydria one wishes to effect. Doses in excess of this tend only to emphasize the disadvantages incident to the use of the drug. It should never be forgotten that the neutralizing power of the magnesia radical is three and a half to four times as strong as that of the soda radical. The same rules that apply to magnesium oxide apply in general to magnesium carbonate, ammoniomagnesium phosphate, the soluble magnesium hydrate, and other magnesium preparations.

The exhibition of magnesium salts at the end of digestion effectually diminishes acidity and has a prolonged action.

The method of administering fractional doses of magnesia at intervals during digestion has proved to be the most practical manner of employing such a salt for the correction of hyperchlorhydria. Five grains of magnesia every half-hour is an excellent antacid for this purpose. The success of the fractional method of administering alkalies confirms the opinion of Bourget,[11] who suggested a saline-alkaline mixture to be sipped at frequent intervals after a meal. He proposed the following formula: ℞—Sodii bicarb. puriss, 8; sodii phosphatis sic, 4; sodii sulphatis sic, 2. Misce fiat pulv. dent. tal. dos. Nr. x. Sig.—One powder dissolved in 1 liter of cold water.

The action of bismuth as an antacid is a highly satisfactory one. The neutralization of the acid is deliberate, moderate and prolonged, and a secondary rise of acidity is avoided. Bismuth subcarbonate has only 36 per cent. of the neutralizing power of an equal quantity by weight of sodium bicarbonate. The breaking down of bismuth subcarbonate to bismuth oxychloride takes place slowly, and it is probably because of the slow decomposition that a secondary acid reaction is prevented.

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seen only in cases of pure hypersecretion. The same disappointment applies to atropin given by mouth even in a single dose or in successive doses during the day. On the other hand, the efficacy of atropin administered hypodermically in cases of hypersecretion accompanying hyperacidity was quite evident. In these cases the acidity was diminished, and in addition the secretion of the gastric tubules was markedly inhibited.

The combination of a more slowly acting antacid, such as bismuth, with the more rapid and vigorous salts of magnesia or soda, is justified by the foregoing experiments. The antacid effect of the bismuth was observable throughout the secondary hyperacid stage produced by the more readily dissociable elements. As regards dosage, the same rules apply to drugs in combination as when they are singly administered. The dose should be a moderate one in both instances.

It becomes apparent from a closer study of these charts that a delay in gastric motility occurs as part of the action of the antacid salts. When moderate doses were used a partial neutralization of the free acidity tended to "slow down" the rate of activity of the gastric ferments. When larger doses were used paralysis of the proteolytic ferment (pepsin) was brought about and proteid digestion temporarily ceased. This, in itself, is a plausible explanation of the delay of motility. Basing one's judgment on the theory of the acid control of the pylorus as propounded by Cannon, one would be led to believe that the diminution of acidity would encourage a patulous pylorus and a more rapid emptying time. But the secondary rise in acid acts in a contrary manner to control and to delay this premature evacuation; the rising acidity toward the end of digestion in place of the customary declining acid values naturally tends to inhibit the emptying of the viscus. However, the delay was rarely prolonged and did not become at any time a considerable factor.

The natural secretion of mucus in the stomach is not apparently affected by the administration of the antacid medicaments.

The regurgitation of bile and duodenal juice, an occurrence which normally takes place in a large proportion of cases, varies only in a manner to parallel the fluctuations in acidity. This regurgitation is not a constant factor and may take place coincidently with a high acidity as well as with a moderate subacidity. The favorite time for the reflux flow of duodenal contents is toward the latter half of digestion, that is, during the period of declining acidity. After the administration of magnesia or bicarbonate, the secondary rise of acid may check this regurgitation of intestinal fluid. Whether this has at the present time any importance or significance, it is impossible to state.

CONCLUSIONS. In general one must feel surprise and disappointment upon realizing the mode of action of the antacid agents, more

particularly the alkaline salts. It is immediately obvious that much misuse of these therapeutic potentialities has taken place in my experience, as well as in the hands of others. With too small a dose no beneficent neutralization is accomplished, while the attendant secondary rise in acidity rarely fails to assert itself. When too large a dose is employed one risks paralyzing the digestion for a considerable period, following which there appears a hyperacidity of even greater degree than the one we undertook to combat. The combination of slowly acting, with more rapid alkalies, is desirable. Atropin has a restricted use and should be employed only as a desiccating agent in instances of hypersecretion.

The use of fractional doses of the alkalies distributed over the course of digestion is the most efficient and physiological method for the employment of these agencies; for this purpose magnesium oxide is the most dependable and best suited salt.

Based upon these studies it seems very questionable whether prolonged use of the alkalies leads to any permanent diminution of the acid secretion of the stomach; in fact, it is as likely that the opposite effect is produced.

A lasting relief of hyperacidity is not to be sought in antacid medication, nor in olive oil or atropin. It is more likely to be found in the proper regulation and restriction of dietary errors as well as in the general control of the hygiene and manner of living of each individual patient under our professional care.

RELAPSING FEVER ENDEMIC IN COLORADO.*

By James J. Waring, M.D.,
DENVER, COL.

When peace is declared the returning flood tide of Americans whom the business of war has called to foreign shores will bring with it necessarily the menace of new diseases now rare or perhaps unknown in the United States. At this time, when the wave of humanity is still moving toward the other side, it is desired to report a case of relapsing fever, a disease all too common in Europe but exceedingly rare in this country.

The following case is important not only for its own sake, because of its rarity, but because the infection was contracted undoubtedly in the same locality as Meader's cases, reported two years ago.

At the Annual Meeting of the Colorado State Medical Society, October 5, 1915 Meader[1] presented clinical histories of 5 cases of relapsing fever, in 2 of which he had found the spirochete. This

* Read before the Medical Society, City and County of Denver, October 13, 1917.

most valuable observation represented the first report of this disease in Colorado. Neither before nor since have any other cases been recorded in this State. Indeed it is many years since relapsing fever has been proved beyond question in American residents of the United States, although it has been found in a few instances among recently arrived immigrants.

Todd[2] says the disease is not endemic in North America. Osler[3] mentions its occurrence in epidemic form in New York and Philadelphia in 1869, adding—"since when it has not reappeared."

Carlisle[4] in reporting 2 cases of relapsing fever in May, 1906, writes—"there are no other cases on record in this country up to the present time in which Sp. obermeieri has been found in the blood." The origin of one of his cases (an Englishman and ship steward) was undoubtedly tropical America. The other was a case of accidental infection of a laboratory worker (the joint author of a paper[5] on this subject in the same journal) from an inoculated monkey. The geographical data incorporated in this paper of Carlisle are most complete.

Clymer[6] credits the Irish immigrants with bringing the disease to Philadelphia in 1844, all of the 15 cases under his care crossing the ocean in the same vessel. A. Dul ois[7] reported a study of 15 cases in 1848. Austin Flint[8] published a lecture in 1870 based on his experiences with the disease in the wards of Bellevue Hospital. To his article was appended a statistical report of 103 cases by T. J. Moore.[9]

The disease appeared in epidemic form in New York in 1869 and continued throughout the year and the next, gradually disappearing in 1871. This outbreak was confined chiefly to Philadelphia and New York, although a few cases were found in Washington, in Maryland, in New Jersey and in Connecticut. One case was imported into Boston as noted in the American translation of Strümpell's work on the *Practice of Medicine*.[10]

In September, 1874, a severe epidemic[11] was observed at Oroville, California, among chinese laborers. This epidemic resembled both *typhus exanthematicus*, or ordinary typhus fever, and *typhus recurrentis*, or relapsing fever. It was probably the latter, but there is no conclusive evidence, as Obermeier[12] did not publish his observations until 1873, although he found spirochetes in the blood of a patient in 1868.

Ward[13] reports a case in an Armenian in Worcester, Mass., in 1899. However suggestive clinically, the diagnosis was not confirmed by the blood examination.

It will then be noted that until Meader's cases were placed on record there were no instances that I have been able to find of this disease with the spirochete demonstrated in the blood originating in the United States among native Americans.

Meader concluded his paper in 1915 as follows: "These cases are

reported for the purpose of calling attention to the existence of this disease in Colorado so that the members of this Society may be

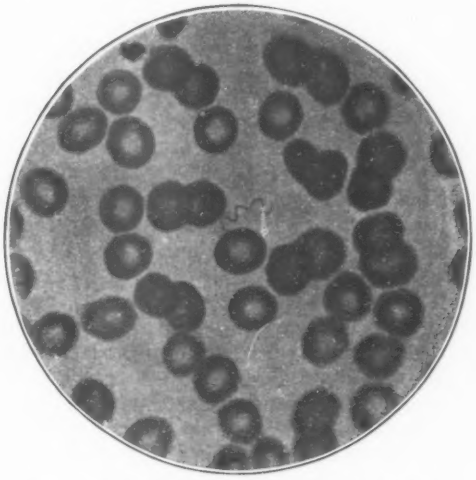

FIG. 1.—Spirochete in the blood. (Meader's case.)

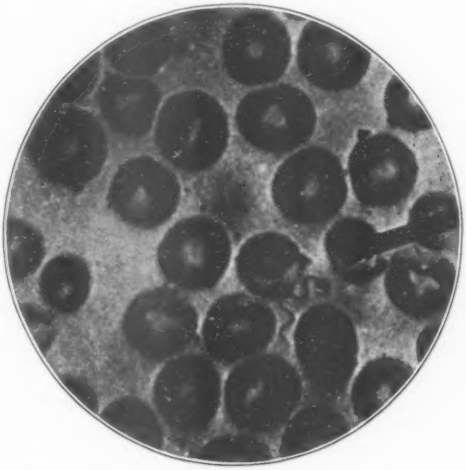

FIG. 2.—Spirochete in the blood. (Waring's case.)

especially on the watch for it to determine if this be only a sporadic accidental outbreak or if we have an endemic focus."

The case whose clinical history follows is placed on record as proving beyond doubt the presence of such an endemic focus in or near Bear Creek Cañon, Colorado.

The patient, a native American, was a boy, aged twelve years. His father has been ill for the past three years with pulmonary tuberculosis and is now an arrested case. The boy himself was examined two years ago by A. C. Foster and G. B. Gilbert, of Colorado Springs, and by them considered to have a slight glandular and pulmonary infection. While under my care this past winter he showed definite evidences of tuberculosis. He came to Colorado July, 1915, and has not been out of the State since except from October 1, 1916, to October 25, 1916, when visiting in Kansas City. He resided in Colorado Springs continuously from his arrival, and saving only for this above-mentioned visit, until he came to Denver, March 12, 1917. July 6 to July 9 he spent at Lake Wellington near Buffalo Park. From August 1 to August 7 he was at Troutdale, Bear Creek Cañon, returning to Denver on the latter date and was taken sick August 12. As the incubation period rarely exceeds eight days the infection must have been contracted at Troutdale.

On Sunday, August 12, the boy was drowsy and disinclined to play. On August 13, he had a chill in the early morning and temperature rapidly rose to 104°. On August 14 it went to 105.2°. By August 16 it had returned to normal. I saw him first on August 13. He was torpid, skin very sallow—almost icteric, eyes bright, cheeks flushed, a herpetic eruption on his upper lip, tongue coated, breath heavy, and complaining bitterly of headache and pains through the back and legs. He also had pain and tenderness over the spleen which was markedly enlarged. The liver was not notably increased in size, nor were heart and lung findings different from former examinations. Bowels were constipated, he had vomited twice and did so repeatedly during this attack and subsequent paroxysms. I might note here that the spleen was palpable throughout his illness but increased considerably in size during the paroxysms, becoming smaller but still palpable in the intervals.

WHITE BLOOD COUNTS.

	8/14	8/24	8/31	9/4	9/10
White cells	6400	7200	9000	8200	12,900
Polymorphonuclears	..	57	62	58	69
Large lymphocytes	..	15	13	2	7
Small lymphocytes	..	11	18	40	23
Transitionals	..	15	7	0	1
Eosinophiles	..	2	0	0	0
Basophiles	..	0	0	0	0
Absolute lymphocyte count	..	1872	2790	3280	3870

In spite of the acute onset typhoid fever was considered a possibility, this suspicion being warranted more or less on the grounds of an enlarged spleen and a leukopenia. The Widal test and blood

culture were both negative and as these reports came in from the laboratory the first crisis occurred, the temperature falling rapidly with moderate sweating to normal. With the subsidence of fever, appetite returned and the malaise disappeared as if by magic. I confess to being puzzled by the return of fever on August 20. On this day he had a hard session with the dentist in the morning, with gradually rising fever in the afternoon. The lung findings were as before except for the presence of deep-seated, distant, subcrepitant rales scattered over the right back and heard only after cough. In this connection Hagler[14] writes that fine moist rales were found in the chest frequently throughout the first few days of the febrile period. There was no cyanosis, pulse 120, eyes and reflexes normal. The spirochetes—probably Spironema novyi were found by my associate in the laboratory, Dr. Ward Burdick, searching at my suggestion, during the second attack. They were overlooked at the first paroxysm but found in these slides on careful subsequent examination.

There was an absence of the urinary findings noted by Meader. I refer to the appearance and disappearance with the paroxysms of a considerable amount of albumin and large numbers of fine hyaline casts. Albumin was found only during the fourth paroxysm.

The differential and total white blood counts are tabulated. Meader calls attention to a rise in the transitionals during the attack and a slightly increased white count and fairly normal differential count during the interval, with corresponding inverse variations in the polymorphonuclear neutrophiles. The counts in this case were made at irregular times in relation to the paroxysm so that deductions are difficult, but it would appear on careful study that Meader's findings are not altogether borne out. One fact is strikingly evident. There is a steady increase in the absolute lymphocyte count. In this connection it will be recalled that Novy and Knapp,[15] who with Gabritschewsky[16] contributed much to the study of immunity in this disease, consider the role of the mononuclear phagocytes most important in the ingestion of dead and enfeebled spironemata under the influence of immune bodies.

The third paroxysm came on August 29, after three days of fever to as high as 99° with the crisis on August 31. There was then an interval of nine days with temperature to 99° or slightly over before the next paroxysm. That the boy was not well during the second and third intervals was evident from the fact that his spleen was still palpable and that he had an occasional elevation of temperature to 99° or slightly over.

Seven days after the third attack there began a mild febrile movement, the high daily point being from 99° to 99.5°. The crisis with fever to 104° plus came on September 9, with normal temperature again on September 11. Exactly seven days after the subsidence of this attack, or on September 17, the temperature was 98.1° at

7 A.M.; at noon it was 99.5°; by 4.30 P.M. it had risen to 110.8° and by 10 P.M. was just short of 105°. Four hours later, or at 2 A.M., of September 18, the temperature was 98.2° and it has remained within normal limits ever since. The patient, somewhat thin and weak after his illness but otherwise in excellent condition, was kept in bed until twelve days had elapsed without fever before permitting him to get up, it having been the general experience[17] that if this interval elapses without a paroxysm none is likely to occur.

DISCUSSION. As transmitting agents bed-bugs, head-lice, body-lice, ticks, fleas and biting flies have all been suspected. Flügge, in 1891, was probably the first to suggest the possibility that vermin might convey relapsing fever in Europe. "Only once have spirochetes been transmitted by the bites of bed-bugs" says Todd. He thinks this was not a true transmission by inoculation but the spirochetes were carried mechanically on the mouth parts of the bugs.

Cuthbert Christy,[18] in India, in 1902, allowed himself to be bitten without becoming infected by bed-bugs caught in the bed of a patient ill with relapsing fever.

Noguchi[19] in a recent exhaustive consideration of sporochetes says: "in the case of *Spironema recurrentis* both body-lice and bed-bugs may be infected by sucking the blood of a patient suffering from the European relapsing fever, but the lice alone can transmit the disease to the next person they bite. Bed-bugs are never known to spread the infection by their bites, although by crushing the infected bugs directly over a minute skin trauma (scratch, etc.), a person may become infected." Breinl and Kinghorn,[20] among others, failed in their attempt to transmit spirochetosis by bugs.

Hagler[21] is inclined to ascribe to the bed-bug a definite and more important role. From a large experience in Serbia he has the following observations to make: Typhus and relapsing fever appeared coincidently in Serbia, and the same preventive measures were effective against both. Typhus fever practically disappeared as the lice were exterminated but relapsing fever persisted until fumigation of rooms and wards with sulphur was undertaken to destroy the bed-bugs, after this it disappeared. Of 50 Red Cross surgeons and nurses at least 20 contracted typhus while none developed relapsing fever. Typhus is admittedly conveyed by the louse and probably more nurses and doctors were bitten by lice than by bed-bugs. These latter have been shown to harbor the *Spironema recurrentis* for as long as sixty days[22] but as noted above, according to Noguchi and other investigators they do not transmit the disease.

The *Pediculus corporis* carries European relapsing fever, but even as close a relative as *Pediculus capitis* has been shown by Gonder[23] to be incapable of spreading the disease, although its body may contain the organisms.

Robledo[24] thinks *Argas americanus* is the tick responsible for the spreading of *Spironema novyi* in Columbia, but this needs confirmation.

Hagler says the tick in Serbia could be excluded as a vector because of its rarity.

In conversation with Dr. Meader I learned of certain ideas of Prof. Theo. D. A. Cockerell, of the University of Colorado, as regards the biting fly as a transmitting agent. The following facts I obtained through Prof. Cockerell. There occurs during the summer months in the mountains of Colorado a powerful biting fly, by name *Symphoromyia*. This fly is found also in the mountainous districts of Europe where relapsing fever occurs. The localities where certain genera are found are as follows:

S. atripes. Rabbit Ear Pass—Long's Peak Trail on way from Long's Peak Inn.

S. hirta. Marshall Pass, 10,856 feet. Long's Peak Trail, on way from Long's Peak Inn. Webber Ranch—between Ward and Allen's Park.

S. pullata. "Colorado."

S. trivittata. "Colorado."

Prof. Cockerell also sent me sketches of the wings of the buffalo gnat and the *symphoromyia*. It is highly improbable that these flies have anything to do with the transmission of this disease. I have been able to find little information on them as possible vectors. Nuttall[25] tried for a long time unavailingly in England to convey the *Trypanosoma brucei* by means of the genus of biting flies called Stomoxys. Schuberg and Kuhn,[26] however, record a successful transmission of relapsing fever by Stomoxys.

How did the disease enter Colorado? It is not only possible but perhaps probable that the band of gypsies mentioned by Meader, that stopped in Bear Creek Cañon at the tent where Meader's patients resided left behind certain undesirable visitors in the form of infected body-lice. Granted this, it follows that the descendants of these pediculi either retained infecting ability from the summer of 1915, until the summer of 1917, a very remote possibility, or other unrecognized cases have come and gone and the said descendants have had opportunity for receiving their infecting store of spirochetes. In any case it seems beyond doubt proved that an endemic form of relapsing fever has been established in Colorado.

REFERENCES.

1. Meader: Colorado Medicine, 1915, xii, 365.
2. Todd: Osler and McCrae, Modern Medicine, 1914, ii, 134.
3. Osler: Principles and Practice of Medicine, 1917, 8th ed., 261
4. Carlisle, R. J.: Jour. Infect. Dis., 1906, iii, 233.
5. Norris: Pappenheimer and Flournoy, Jour. Infect. Dis., 1906, iii, 266.
6. Clymer, M.: Fevers: Their Diagnosis, Pathology and Treatment, Philadelphia, 1846. Notes on the History of Relapsing Fever, New York Med. Jour., 1870, xi, 55.
7. Dubois, A.: Tr. Am. Med. Assn., vol. ii.
8. Flint, A.: Clinical Reports on Continued Fever, etc., 1852. A Treatise on the Principles and Practice of Medicine, 1884, 5th ed.
9. Moore, T. J.: New York Med. Jour., March, 1870.
10. Strümpell: Practice of Medicine, 1913, American translation, vol. i, 39.

11. Miller, P. B. M.: Epidemic Relapsing Fever, Pacific Med. and Surg. Jour., 1874–75, xvii, 370.
12. Obermeier: Centralbl. f. d. med. Wissensch., 1873, 145; Berl. klin. Wchnschr., 1873, 152.
13. Ward, G.: A Case of Relapsing Fever, Boston Med. and Surg. Jour., 1900, cxlii, 36.
14. Hagler: Military Surgeon, 1916, xxxix, 36.
15. Novy and Knapp: Jour. Infect. Dis., 1906, iii, 291.
16. Gabritschewsky: Ann. de l'Inst. Pasteur, 1896, x, 629; 1897, xi, 638.
17. Hagler: Loc. cit.
18. Christy: Spirillum Fever (Relapsing or Famine Fever), Jour. Trop. Med., 1902, v, 39. O. Moubata Fever and Tick Fever in Man, British Med. Jour., 1903, ii, 652.
19. Noguchi: Spirochetes, Jour. Lab. and Clin. Med., 1917, ii, 365; ibid., 472.
20. Breinl and Kinghorn: Lancet, London, 1906, i, 668.
21. Hagler: Loc. cit.
22. Karlinski: Fortschr. der Med., 1890, viii, 161; ibid., 1891, ix, 456. Tictin: Centralbl. f. Bakteriol., 1894, xv, 840; ibid., 1897, xxi, 179.
23. Cited by Noguchi.
24. Cited by Noguchi.
25. Nuttall: Herter Lecture, Johns Hopkins Hosp. Bull., 1913, xxiv, 33.
26. Schuberg and Kuhn: I. Teil, Arbeiten aus dem. kaiserl. Gesundheitsamte, 1911, xxxi, 377; II Teil, ibid., 1912, xl, 209.

A VACCINE FOR THE TREATMENT OF BRONCHIAL ASTHMA: REPORT OF TWENTY CASES.[1]

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and
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The work of Auer and Lewis, Meltzer, Vaughan, Babcock and others leaves little doubt that the disease so long known as bronchial or idiopathic asthma has been permanently removed etiologically from the neuroses, and is now fully explained as a manifestation of protein sensitization. The paroxysmal outbursts represent anaphylactic shock and the various causes formerly thought to act reflexly, and whose removal often resulted in cure, are now believed to be foci from which the foreign material necessary to induce an attack is elaborated.

Judging from the widely diversified nature of the exciting causes of asthmatic seizures it would seem probable that the specific poison either occurs in a number of forms or is common to a great variety of plants and animals as well as bacteria. Moreover, from our understanding of the conditions underlying sensitization it is evident that an immunity could be produced provided the specific protein was capable of being isolated in an available form and

[1] Read before the Nineteenth Annual Meeting of the Tri-State Medical Society, at Durham, N. C.

injected into the sensitized individual in suitable amounts and at proper intervals. This procedure, however, assuming that it was possible in more than a limited number of cases, would involve an amount of time and work far exceeding the means of the average sufferer from asthma.

Certain observations of the writers, derived from the study of a considerable number of cases of asthma, have strongly suggested the possibility of the presence of the specific protein in the bronchial secretions of the patient himself, and also that this protein may be recovered in suitable form for use in bringing about immunity.

In the fall of 1915 we began to prepare vaccines for asthma cases along the lines suggested by Babcock. From our first patient we succeeded in growing the organism described by him, along with a few streptococci and staphylococci. The result in this case was truly remarkable. The second or third injection was sufficient to give immediate and absolute relief for a period of a year. In our second attempt at sputum growth from an asthmatic we failed to grow Babcock's organism and despaired of making up the vaccine because of the fact we were led to believe from his results that his organism was specific for this condition. We did, however, prepare a vaccine from the growth which contained streptococcus, staphylococcus and Micrococcus catarrhalis along with a small amount of broth-culture media. The result in this case was even more striking than the first. Our third case was treated with the mixture of the broth sputum and the bacterial flora, and the outcome of the treatment was equally as startling. We then abandoned the anaërobic method of culture and commenced to grow our organisms by aërobic methods. More recently we have been adding a drop or two of guinea-pig serum along with the sputum and broth and incubating the whole for a period of forty-eight hours before making up our vaccine.

Our present vaccine is made in the following manner: 1 c.c. of washed sputum is incubated in 10 c.c. of broth and 1 or 2 drops of guinea-pig serum for a period of forty-eight hours. At the expiration of that time the culture is standardized and killed by heat of 60° C. for a period of two hours. Further decomposition is prevented by adding carbolic acid until a 1 per cent. solution results. This is cultured out to ensure sterility of our suspension. The vaccine is then diluted with normal saline until each cubic centimeter of the suspension contains 500,000,000 to 1,000,000,000 organisms. The initial dose is 5 minims and each subsequent dose is increased by 1 minim. We do not increase beyond 15 minims, although we may continue the treatment several weeks after this amount has been reached.

At first glance this mixture seems to be a gunshot one, but a more careful survey of its constituents and the results obtained by its administration should, in our opinion, warrant its use. It

is quite possible that the anaphylatoxin that is responsible for asthma may be produced *in vitro*, and that the proper administration of this anaphylatoxin may give a relative immunity to further intoxication.

Friedberger succeeded in producing toxic substances *in vitro*, and these gave rise to typical anaphylactic symptoms when injected into normal animals. In later experiments, however, he obtained similar poisons from bacteria and other proteins by their incubation with normal guinea-pig complement without the concurrence of a specific antibody; while other observers have been able to isolate similar poisons by the incubation of normal guinea-pig serum with starch, agar, etc., and have decided that the poison originated from the serum. Friedberger, however, objected to this on the grounds that the small amount of protein impurities in the agar and starch furnish the material for the formation of the anaphylatoxin.

The exact nature of asthma anaphylatoxin then is still unknown, but it is reasonable to believe that the anaphylactic symptoms are produced by the digestion and the split products of the sputum, bacteria, etc.

It has been observed that animals receiving injections of a foreign protein at short intervals develop a decided resistance to this substance, so that several lethal doses for a sensitized animal may be given without producing symptoms. If, however, the time between injections is sufficient to sensitize the animal anaphylactic shock will result. In other words, frequent doses at short intervals will confer an immunity to a protein, while if the dose is spaced over a period of eight to ten days the animal becomes hypersensitive. In giving vaccine we attempt to raise the resistance of our patients against the anaphylatoxin of asthma. In other words, we vaccinate against anaphylaxis, and the resulting state might be called anti-anaphylaxis.

We have been able so far to observe the effect of this plan of treatment in 20 cases of typical bronchial asthma.

In 12 of these cases complete relief from attacks was experienced after from one to five injections of the vaccine and this relief has persisted up to the present time. The longest period of freedom from symptoms is sixteen months, the shortest six weeks.

In 5 cases distinct improvement has been noted either in the frequency of the seizures, their severity, or their duration. In 3 of these cases improvement occurred only after a second vaccine had been made and administered at shorter intervals than the first.

In 2 cases no effect at all was produced. One of these patients was an elderly man with emphysematous lungs and a history of asthma extending over twenty years. Asthma in the other case had followed injury to the chest and roentgen-ray examination revealed ununited fractures of several ribs.

In 1 case administration of the vaccine seemed to increase the

intensity of the paroxysms, a result which appeared to be explained by the fact that too long a time was allowed to elapse between injections.

Injections have in most cases been made twice a week. We are of the opinion, however, that a shorter interval will prove more desirable. We have also attempted, in each case, to remove an obvious focus of infection, but have refrained from any other treatment while the vaccine was being used.

We have been greatly impressed by the above results and hope to determine in the near future (1) whether or not the elements constituting the mixture are effective if injected separately; (2) also which element is potent; (3) and whether the protein injected is specific or not.

A STUDY OF ATMOSPHERIC AIR IN THE UPPER DIGESTIVE TRACT.*

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It is only within recent years that sufficient attention has been accorded to the role played by atmospheric air in the physiology and pathology of the digestive tract. Although the symptoms associated with the presence of gas—belching, tympany, meteorism, flatulence, etc.—have been the subject of comment from the earliest times, it has most commonly been taken for granted that the gases in question have had their origin entirely within the body, whether from the decomposition of food, the exhalation of vapors or from the interplay of gas-producing juices. It would seem therefore advisable, before presenting any observations based on newer methods, to pass in brief review the more important of the many scattered observations of earlier writers.

I. HISTORICAL BACKGROUND.

Interest in the subject dates back to the time of Hippocrates, to whom is ascribed a book on the "winds" or "flatuosities."[21] Following this authority, many of the ancients created an entity of the condition, to which they gave the name *morbus ructuosus*, and ascribed all sorts of disorders to it. These men became known as "pneumatists." This doctrine was energetically opposed by Combalusier (1747),[11] who attempted to give a more restricted significance to the role played by the gases.

* Read in part under the title of "The Physiology of Aerophagia," at a meeting of the Section on Medicine of the New York Academy of Medicine, December 18, 1917. Dr. Meltzer discussed the paper and his remarks are published in the Medical Record, 1918, xciii, 100.

Although as far back as 1652 a study of the intestinal gases had been made by Van Helmont,[19] it was not until the end of the eighteenth century that the indefinite notion of *morbus* was abandoned and that interest was centered on the actual composition and origin of the gases (Jurine (1789),[25] Gerardin (1814),[17] Magendie and Chevreul (1814),[32] Vauquelin (1817),[51] Lameyran and Fremy (1819),[29] etc.). As material, both humans and animals were used. The human subjects were examined apparently only postmortem, freshly executed criminals being common objects of study. Despite the presumably crude methods employed, the basis for the chemistry of the subject was really laid down in these investigations.

At this period also we have the first clear account of air-swallowing in Magendie's report of the case of a conscript who practised autoinflation in order to avoid military service (1813).[76] In 1832 Baumès[4] published a series of letters in which he strongly advocated the view that under appropriate irritation the mucous membranes could give rise to a gaseous flux, just as they do to a mucous or serous or hemorrhagic flux—*ubi stimulus, ibi fluxus*. This work is the historic basis for the theory of "alimentary respiration."

With the exception of the careful quantitative studies of Chevillot (1833)[8] on the gases of man in health and disease, not much of importance was added by French scholars until the renewed interest in air-swallowing late in the nineteenth century. On the other hand, German workers began to contribute extensively to our knowledge of the gases of fermentation. Apparently their interest was first directed in this channel by the discovery that inflammable gases may be present in gastric contents* and a rather rich literature was created on this subject alone (Carius (1865),[7] Popoff (1870),[42 43] Emminghaus (1872),[14] Ewald (1874),[15] Schultze (1874),[47] Heynsius (1874),[20] Poensgen (1879),[41] Korach (1880)[26]). These investigations were expanded until the whole question of gastric fermentation and putrefaction was covered, not only from its chemical aspect, but from the bacteriological and general clinical view-points as well (Naunyn (1882),[39] Miller (1885, 1886),[34 35] Minkowski (1885),[37] Riegel (1892),[44] Kuhn (1892),[27 28] Hoppe-Seyler (1892),[22] Boas (1892),[6] McNaught (1893),[33] Straus (1894, 1896),[48 49] Dallemagne (1895),[12] Mills (1896),[36] Basch (1908)[3]).

Interesting as this work is, it should be noted that in the last analysis it throws light on but a single pathological condition, namely, pyloric obstruction with gastric fermentation and putrefaction, and that it gives but indirect evidence, if indeed any, as to the ordinary sources and behavior of the gastric gases. Of really greater importance for this purpose are the experimental contributions of Planer (1860),[40] Tappeiner (1882),[50] Schierbeck (1892, 1895),[45 46] Giglio

* "Als (Patient) beim Anstecken einer Cigarre zufällig aufstossen musste, zum ersten Mal zu seiner nicht geringen Verwunderung die Brennbarkeit seines Ructus constatierte, und immer wieder . . . demonstrieren konnte." Ewald.[15]

(1905),[18] Woodyatt and Graham (1912),[53] and Yllpö (1916).[54 55] The general trend of most of this work is toward the belief that the basis of gastric gases under normal conditions is constituted by atmospheric air, modified in its composition by certain definite processes to be described later in this paper.

Mention has already been made of the work of Magendie. This illustrious physiologist pointed out that air-swallowing was akin to the "cribbing" of horses, that the condition was by no means a rare one—he found it in at least eight out of one hundred students examined—and that it could be acquired by practice. He also made the first attempt at describing the mechanism of the act itself. Despite the publication in the succeeding years of several special articles on the subject (Pierquin (1830),[82] Heusinger (1862),[67] Falke (1863),[65] Piorry (1871),[83] Weissgerber (1878)[94]), as well as the mention of air-swallowing as a possibility in some of the general medical works of the period (*e. g.*, Chomel (1842),[9 10] Andral (1848),[1] Luton (1870),[30 31] Eichhorst (1887)[13]), it was never fully realized that air-swallowing is a perfectly normal physiological process, nor that under pathological conditions it may give rise to disturbances generally assumed to be due to gases originating within the body.

Indeed, it was not until the publication, in 1889, by Quincke[85] and in 1891 by Bouveret[58] that the present view-point was given complete expression. Bouveret's term "aërophagia" was immediately accepted and confirmatory papers followed each other quickly (Rosenbach (1889),[86] Aubert (1891),[57] Pitres (1895),[84] Obici (1895),[80] Vauthey (1896),[52] Vincens (1900),[93] Linossier (1901),[73] Lyonnet and Vincens (1901),[75] Mathieu and Follet (1901),[77] Soupault (1901),[89] Bouveret (1901),[59] Perrody (1902),[81] Morange (1903),[79] Mathieu (1904),[78] Spivak (1905),[88] Dobrovici (1906),[62] Ewald (1910),[16] Thomas (1912),[91] Leven (1913),[71] Bucholz (1913)[60]). Roentgen-ray observations have been reported by Abrams (1898),[56] Variot (1901),[92] Hoffmann (1905),[68] Soupault (1906),[90] Lesage, Levèn and Barret (1908),[70] Leven and Barret (1909),[72] Thomas (1912),[91] Eisler and Kreutzfuchs (1912),[64] Kraus (1912, 1913),[107 108] Barclay (1913),[57 bis] Leven (1913),[71] Smith and LeWald (1915).[87]

II. THE NATURE AND ORIGIN OF THE GASES ORDINARILY PRESENT IN THE STOMACH.

Although it is perhaps now generally recognized that air is constantly being swallowed by normal individuals, it is not so widely admitted that the gases of the stomach are derived entirely from the atmosphere. Clinicians have long puzzled over the nature of certain violent outbursts, in patients proved to be free from gastric fermentation, of acute meteorism, generally associated with eructations of apparently enormous quantities of gas. Some writers have attempted

to include all such cases under the head of aërophagia, and Buchholz[60] has devoted a thesis to the proof that even the most severe forms (acute gastric dilatation) are nothing but aërophagia run riot. Others have from time to time advanced the hypothesis that there is sudden nervous relaxation of the pylorus with regurgitation of (preformed) intestinal gases or of alkaline duodenal contents (Benedict[5]) into an acid stomach with a consequent liberation of carbon dioxide. To be sure, Hoppe-Seyler[22] did find increased amounts of CO_2 in the stomach in the presence of duodenal regurgitation, and the explanation as advanced cannot be denied *ex cathedra*. However, the experimental evidence thus far available seems

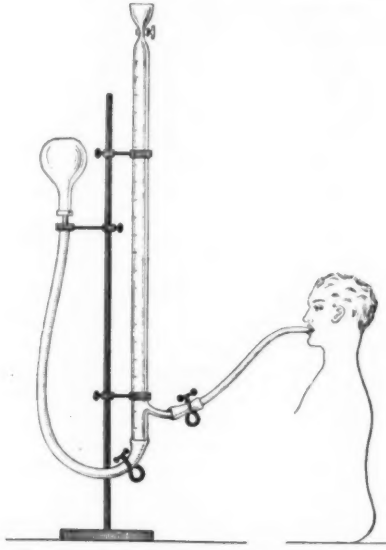

FIG. *A*.—Hoppe-Seyler's apparatus for analyzing the gas of the stomach.

opposed to this view, for Schierbeck[45] found that the gas values obtained in the stomach under various conditions were the same whether the pylorus was artificially closed off or not, and Dobrovici[62] showed that the pressure in the small intestine can be increased without regurgitation until, at 40 cm. of water, it is the ileocecal valve and not the pylorus that gives way under the strain.

On the other hand, a third theory, already mentioned under the name of "gastric or alimentary respiration," deserves more detailed consideration. If the gaseous constituents of a normal stomach are removed and analyzed, generally nothing but oxygen, nitrogen, and carbon dioxide will be found in proportions approximating, but

never quite the same as, those of atmospheric air. This investigation may be carried out in several ways. Perhaps the simplest, though possibly the crudest manner, is to collect the gas of eructations directly, as was done by Ewald and Rupstein[15] in their case of pyloric obstruction. Another method is to introduce a tube and obtain the entire contents of the stomach (Hoppe-Seyler,[23] Yllpö[54]). In animals more elaborate procedures can be carried out. Thus Schierbeck, in his classic studies of CO_2 tension,[45 45] filled the stomach with water, withdrew the fluid after an interval sufficient for complete absorption and estimated the CO_2 after driving it off by boiling into a standard baryta solution. Woodyatt and Graham,[53] in their confirmatory investigations, preferred to fill the stomach with air and to estimate the CO_2 carefully in the resultant gas mixture. Giglio[18] punctured the stomach directly and thus obtained gases absolutely free from secondary air contamination.

In a few preliminary estimations* undertaken on an unselected series of individuals aspirated at various intervals after eating, I obtained the following values:

Specimen.	Gas recovered, c.c.	CO_2 per cent.	O per cent.	N per cent.
1	49.5	4.4	19.1	76.5
2	12.2	4.1	13.6	82.3
3	36.9	6.2	18.5	75.3
4	48.2	2.0	17.0	81.0
5	43.4	4.1	17.2	79.0
Average	39.6	4.16	17.08	78.82
Inspired air (after Howell)		0.04	20.96	79.0
Expired air (after Howell)		4.38	16.02	79.0

These figures confirm those originally reported by Hoppe-Seyler[22] on the aspirated gases of non-obstructed cases as well as those reported by Pitres,[84] by Soupault[89] and by Linossier[73] on the gases of eructations.

The striking feature in all these results is the relatively high pro-

* The apparatus employed was the simpler one of the two devised by Hoppe-Seyler,[23] the stomach contents being obtained by aspiration with an Ewald bulb, instead of by siphonage with a funnel as originally recommended (see Fig. *A*). The outfit consists essentially of a graduated tube (in which the gases are collected and analyzed) provided with two wide outlets at the bottom, and a narrow one at the top. The uppermost opening, closed off by a stop-cock, is connected with a thistle funnel through which the necessary reagents are admitted. The upper of the two lower apertures is connected with the stomach-tube (single opening at the end) and the lowermost of the two with the aspirator. Both can be closed off with pinch-cocks. The entire apparatus, including the stomach-tube, is filled with water, the end of the tube being sealed off with a plug of vaseline, and the exhausted aspirator is attached to the distal end of the system. The tube is then introduced into the stomach, and aspiration commenced. The gas volume may be read off directly from the graduations. The CO_2 is absorbed in 20 per cent. KOH, the oxygen in strongly alkalinized pyrogallol solution. The nitrogen is estimated by difference. These experiments were performed in the summer of 1916 in the Laboratory of the Department of Physiology of Columbia University. It is a pleasure to acknowledge the kind interest of Professor Lee and his generosity in providing the necessary apparatus.

portion of carbon dioxide. This gas obviously cannot come from admixture with expired air, for it occurs in amounts equal to if not greater than the latter. What, then, is its origin?

As early as 1814 Gerardin and Magendie[17] tied off loops of intestine in dogs and found an accumulation of gas which they attributed to vital secretion of the mucosa. As already mentioned this theory was elaborated particularly by Baumès in 1832.[4] It received still further confirmation from the animal experiments of Planer in 1860,[40] who found that the stomach absorbed oxygen and secreted carbon dioxide in the proportion of two parts of the latter to one of of the former. Subsequently, however, the view that a direct secretion of CO_2 takes place was abandoned, and it was generally assumed that the oxygen and the nitrogen of the stomach gases come from the swallowed air, whereas the CO_2 arises from the blood by simple diffusion. In 1892 Schierbeck[45] made an important series of experiments, using the method described at the beginning of this section. This author found that CO_2 is always present in the stomach and that its tension varies directly with the stage of digestion. Beginning with 30 to 40 mm. in the fasting animal the CO_2 tension rises to 130 or 140 mm. at the height of gastric activity. Schierbeck therefore rejects the view that the CO_2 results from diffusion (for its tension in the cavity of the stomach is far higher than it is in the gastric vessels*) and concludes that the gas is an expression of the metabolic activity of the gastric mucosa. In other words, he has furnished a strong experimental basis for the old theory of alimentary respiration.

These studies have been extended by Giglio,[18] who found that the production of CO_2 is considerably influenced by the kind of food ingested, the carbohydrates causing the greatest production of the gas, the fats the least. In normal dogs he could not confirm the classic 1 to 2 ratio of Planer, but found values ranging from 1 to 1.30 to 1 to 0.67 according to the diets used.

From the work quoted it cannot longer be doubted that some of the gas (CO_2) normally present in the stomach arises from the gastric mucosa itself. What evidence is there that this gas may at times be produced in such amounts as to cause gross pathological accumulations? Bardet[2] has studied 2 cases of occasional flatulence. He recovered 20 to 50 liters of gas in one hour, and this gas contained on an average: CO_2, 80 per cent.; O, 7 per cent.; N, 13 per cent. Woodyatt and Graham[53] found in a case of acute gastric dilatation: CO_2, 24 per cent.; O, 4 per cent.; N, 72 per cent. Experimentally Schierbeck[46] showed that the low CO_2 tension of a fasting animal could be increased by injections of pilocarpin and that the high tension of a fed animal could be depressed by injections of nicotin. A high CO_2 tension persisted unchanged after vagus section. Unfor-

* The average CO_2 tension of arterial blood is 35 mm. Hg. (Howell[24]).

tunately, further direct experiments on the nervous control of gas production are wanting.* The entire question must really be studied much further before we can speak with real confidence of these abnormal gas productions.

III. THE ENTRY OF AIR INTO THE STOMACH; AIR-SWALLOWING.

If any sufficiently large group of individuals be examined it will be found that perhaps a majority will recall that they belch after eating.† A smaller number will be able to belch on request. A very few may be able to swallow air when asked to do so. In addition a certain proportion will be found to be unconscious belchers and air-swallowers, whereas a final group will be quite unable to belch or to swallow air even after making every effort to acquire the practice. It is important for the student of the physiology of air-swallowing to bear these facts in mind, for we are about to enter a field in which there is every gradation between the distinctly conscious or volitional on the one hand and the subconscious, automatic or reflex on the other. It is not without reason that the French have described aerophagia as an unconscious voluntary act. This apparent paradox is essentially true, for in the first place no act of air-swallowing can be initiated without the participation of striped or voluntary muscle groups on the one hand, whereas it can be checked or prevented by the influence of the will on the other; and in the second place the process may be repeated so often that it becomes a habit and thus passes into the realm of the subconscious, where it is no longer recognized as a distinct procedure by the subject.

* In this connection it may be of some interest to recall the following observation. As is well known, certain fishes are supplied with air bladders (originally derived from the alimentary canal), and in some of these, highly vascular bodies known as red glands or gas glands, are present. These bodies serve to regulate the interchange of gases in the bladder, and this rudimentary or secondary respiration has often been pointed to as being analogous to the alimentary respiration of the higher vertebrates which we have been studying. A very elaborate study of the function of the air bladder was undertaken by the French zoölogist Moreau.[38] This worker made the interesting discovery that section of the sympathetic nerve to the swim bladder causes an increased production of oxygen, whereas section of the vagus does not affect the oxygen content.

† Among the Orientals, belching in public is not considered out of place, as with us. Thus Morange writes:[79] "Un de nos amis, officier d'infanterie coloniale, ayant pris part à la recente campagne de Chine, nous décrivait comme suit le cérémonial de la fin d'un diner chez un riche mandarin: après le défilé d'une trentaine de plats et l'absorption du riz traditionnel, l'amphytryon se lève et s'excuse auprès de ses invités de les avoir si pitoyablement traités, redoutant que leur faim ne soit pas complètement assouvie. Ceux-ci protestent alors avec véhémence, vantant la delicatesse, la varieté des plats servis; puis, appuyant les mains sur le ventre, ils s'approchent de leur hôte et lui lancent en plein visage plusiers rots bien sonores, temoignant ainsi que leur estomac est bien garni." The following quaint passage from a letter by Flaubert is also *à propos*: "Quelques fois nous nous arrêtons pour déjeuner dans un restaurant turc; là on déchire la viande avec ses mains, on recueille la sauce avec son plain, on boit de l'eau dans des jattes, la vermine court sur la muraille, et toute l'assistance rote qui mieux mieux, c'est charmant." (Quoted by Aubert[57].)

Air may enter the stomach in one of two ways: It may either be carried down with fluids or solids in ordinary swallowing or it may be "gulped" down alone.

THE SWALLOWING OF AIR WITH FOOD. This method of air entry into the stomach occurs to a greater or a less degree in every individual. It is nearly always subconscious. In order to understand the mechanism of this process it is necessary to review critically and in some detail our knowledge of deglutition in general.

The Mechanism of Deglutition. Magendie[113 114] made the first classic studies on the subject and came to the conclusion that a bolus is propelled by peristalsis through three successive portions of the tract, viz., the mouth, the pharynx and the esophagus. Between the years 1880 and 1883 the Berlin physiologists, Kronecker, Falk and Meltzer, carried out a series of brilliant investigations which have served as the basis for our modern knowledge of the subject. Kronecker and Falk[109] found that at the moment of swallowing a pressure of 20 cm. of water is developed in the buccopharynx and that it is propagated onto the esophagus, but is absent in the stomach. Furthermore, by means of balloons in the pharynx and esophagus, connected with a recording drum, Kronecker and Meltzer showed that fluids were projected down almost instantaneously.[110 112] They then presented a theory of deglutition essentially as follows: The swallowing act is initiated by a contraction of the mylohyoids, which develop enough pressure to "squirt" the bolus down the entire esophagus without the aid of peristalsis. After the passage of the fluid the esophagus begins to contract until, at about six seconds, the "wave" reaches the cardia. This contraction serves simply as a reserve means of clearing the esophagus of the last remnants of the original bolus. Further graphic studies were contributed by Schreiber,[126 127 128] who showed that before the esophagus opens to admit the bolus a considerable negative pressure is developed. Instead of reaching the cardia in one-tenth second, as Kronecker and Meltzer supposed, it takes almost two seconds for this period of the act, a figure more nearly in accord with roentgen-ray observations. This first stage of swallowing was studied in greater detail by Kindermann (with Zwaardemaker) (1903),[106] who proposed to divide the entire act of deglutition into two main periods, a buccopharyngeal and an esophageal. The buccopharyngeal period is further subdivided into three phases (*Einstellungsphase*, *Austreibungsphase* and *Regressivephase*) according to the role played by the floor of the mouth, the soft palate, the hyoid bone, the larynx, and the epi- and mesopharynx.

The next important physiological observations were contributed by clinicians. The surgeon, v. Mikulicz,[129] became attracted to the subject through his interest in esophagoscopy. He showed that the esophagus is open and air-containing from the level of

the larynx to the cardia, and that the pressure within the lumen is normally from −0.5 to −3 cm. of water (Schlippe, working independently, gives practically the same figures).[125] Fluids may pass through the cardia into the stomach without the aid of any factor other than gravity alone. In a very thorough study, based on anatomical, pathological and clinical grounds, the laryngologist Killian showed (1908)[105] that the top of the esophagus was closed off from the hypopharynx not only by the dead weight of the opposed larynx but by a very real, tonically contracted sphincteric musculature. To this he gave the name "mouth of the esophagus," and found that it relaxed, by an inhibitory reflex, only on swallowing, retching and vomiting.

The first roentgen-ray observations were made in 1898 by Cannon and Moser,[98] who showed that fluids were projected rapidly (squirted), whereas solids and semisolids were propelled more gradually by peristalsis. These studies were followed by those of Eykman (1903),[99] who directed his attention entirely to the buccopharyngeal period of deglutition. Further roentgen-ray observations have been reported by Hertz (1907),[102] Scheier (1911),[124] Schreiber (1911),[127] Kraus (1912),[107] Held and Gross (1906)[101] and Hirsch (1916).[104] The work of Kraus is particularly important. This observer found, by means of roentgen cinematography, what had indeed been described earlier by Hertz, namely, that the esophageal period is really of more importance than earlier writers had assumed. Instead of the bolus being squirted through the cardia with the initial buccopharyngeal thrust, it passes but slowly into the stomach under the pressure of the esophageal "peristole," and is followed invariably by a bubble of air. It is only by means of a nice interplay of cardiac relaxation and esophageal peristalsis that the bolus is finally delivered into the stomach.

Reviewing the above descriptions of the act of deglutition in the light of his own fluoroscopic observations the writer has come to agree thoroughly with Kraus in his statement that too little importance is generally attached to the phenomena associated with the cardia. This is undoubtedly due to the difficulty encountered in studying this region before the application of the roentgen rays to clinical physiology. It would seem perhaps more in harmony with the latest studies to speak of the swallowing act as composed of three, rather than two, chief periods, viz., a buccopharyngeal period, an esophageal period and a cardiac or cardiogastric period. This would bring into greater prominence such important work as that of Müller and Saxl (1908),[121] who suggested that both the rearrangement of the individual muscle fibers and the relaxation of their tone is due to a reflex from swallowing; as well as that of Cannon and Lieb (1911)[97] who studied this phenomenon experimentally in man and animals, and gave it the happy designation of "the receptive relaxation of the stomach." In other

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words, the act of deglutition is consummated, not with the arrival of the bolus in the esophagus or at the cardia, but with its penetration into the stomach; and the preparation of the latter organ is just as much a part of the process as are any of the phenomena heretofore considered. In fact, we are dealing with an orderly progression of pressures and inhibitions which may be presented, so far as they are known, schematically, as follows:

A. Pressures:
1. Initial buccopharyngeal thrust (Meltzer and collaborators).
2. Esophageal peristalsis (Magendie, etc.).

B. Inhibitions:
1. Inhibition of esophagus mouth (Killian).
2. Relaxation of esophagus (Schreiber).
3. Inhibition of cardia (Meltzer).
4. Receptive relaxation of stomach (Cannon).

From this new view-point, then, the known facts of deglutition may be summarized as follows:

Buccopharyngeal Period: The mouth is closed off anteriorly by the rise of the base of the tongue, the nasopharynx by the rise of the soft palate. The larynx advances and is sealed by the epiglottis and the back of the tongue. The bolus is thrust down by the contraction of the mylohyoids chiefly. This period is completed with the return of the larynx to its original position and is over in less than a second (seven-tenths to one second—Kraus).

Esophageal Period: This period begins almost immediately with the discharge of the deglutition reflex by a relaxation of the entire esophagus. At two-tenths second (Screiber) the esophagus mouth opens just long enough to receive the bolus. After the entry of the latter, peristalsis begins at the closed esophagus mouth and forces down the bolus with its accompanying air bubble. This period ends with the arrival of the wave at the cardia and lasts six to seven seconds in all.

Cardiogastric Period: This period also begins with the discharge of the deglutition reflex, by an inhibition in the tone of the cardia (Kronecker and Meltzer) and a relaxation of the stomach. According to Cannon the lowest point of intragastric pressure is reached at approximately the time when a bolus is delivered into the stomach by the esophagus. After the relaxation, which requires about ten seconds for its full development, there is a rapid recovery of the former tonicity.

It is thus seen that the successive periods overlap, in this way providing for a practically continuous passage of the bolus. The only delay is at the cardia, where the relaxation is never complete enough, normally, for a discharge of the bolus, *en masse*, into the stomach.

Swallowing Sounds. On auscultating an empty stomach in the epigastric region during a single swallow of fluid a very characteristic

sound is heard six to seven seconds after deglutition. This phenomenon was carefully studied by Meltzer* (1883),[116] and was called by him "*Durchpressgeräusch.*" It has become known in the literature also as the "second swallowing sound." Meltzer found that the interval elapsing before the sound was heard corresponded to the time necessary for the wave of esophageal peristalsis to reach the cardia, and he therefore formulated his theory that the bolus, after being shot rapidly through the esophagus, was held up until the succeeding wave of peristalsis forced it into the stomach. If the cardia was relaxed—as was found to be the case in a small minority of individuals—the food went through at once, and a short "*Durchspritzgeräusch*" ("first swallowing sound") was heard correspondingly earlier. The same author also pointed out (1884)[117] that the sound was not heard over the filled portion of the stomach, and that as more food was ingested the murmur became fainter (higher pitched), and finally quite inaudible. Zenker (1884)[130] was the first to advance the theory that as each bolus reaches the cardia it separates into two parts, the fluid constituents going through first, the air following later with a murmur. As proof, he brought forth the fact that in an inverted subject the murmur is heard immediately after swallowing. In 1887 Quincke furnished still more elaborate experimental evidence[123] that the swallowing sound was due to the entrance of air into the stomach. Experimenting with narcotized dogs, he introduced a tube through the esophagus to a point somewhat above the cardia. This tube was attached to a burette in such a fashion that air or water could be introduced at will. It was found that if a normal-sized bolus of air or water was delivered into the esophagus by this means it was promptly propelled into the stomach by the so-called secondary peristalsis of Kronecker and Meltzer[112]—peristalsis not associated with a previous deglutition. When water alone was introduced no swallowing sound was observed; only when air had been previously admitted was the murmur audible. Quincke concluded that the character of the swallowing sound depended upon the amount and consistence of the bolus as well as upon the size and position of the air space in the stomach.

The first roentgen-ray studies of the swallowing sounds were made by Hertz (1907).[102] This author experimented on a group of healthy men and observed that certain changes in the character of the sounds were associated with changes in the position of the

* The first author to mention this sound was Natanson (1864),[122] but his description was very incomplete. Hamburger made an elaborate study of the auscultatory phenomena of swallowing (1868),[100] but listened to the esophagus from behind and did not hear the sound. Allbutt follows Hamburger entirely (1875).[95] The only one who can claim priority to Meltzer was Zenker who described the murmur accurately in 1869.[129] His original paper appeared in a small psychiatric journal and did not receive general recognition.

body. Although he correctly observed that the second swallowing sound was heard just after the food had left the esophagus he failed to give any satisfactory explanation for the phenomenon. Kraus (1912)[107] was apparently the first roentgenologist to make the positive observation that the swallowing sounds are caused by the penetration of air into the stomach, but he has published no detailed account of the subject.

Experimental. In view of the above rather unsatisfactory state of the literature the writer undertook a study of the problem with the aid of the fluoroscope, hoping in this way to establish more precisely the relation between the swallowing sounds and the entry of air into the stomach. As subjects, ten healthy men were selected. These were examined fasting. At practically every session a complete standard opaque meal—100 gm. barium sulphate in two glasses (500 c.c.) of fermented milk—was given so that the conditions could be observed in each individual at every stage of gastric filling. Twenty-one observations were made in this series. The exact procedure was as follows: The subject was placed behind the screen and a preliminary fluoroscopy made in order to note the presence of a fasting *Magenblase* or other gas accumulation in the abdomen. The first glass was then given to the subject to hold in readiness, and he was told to make a single deglutition at the word "swallow" and to strike the operator at the exact time the order was carried out. It was found essential to adopt some such method of announcing the execution of each swallow (whether by command or involuntarily), as it would otherwise have been impossible for the observer to interpret correctly the phenomena occurring at the cardia. Finally, the stethoscope was adjusted in position, the rubber tubing being long enough to reach under the screen to the epigastric notch of the subject. The observations were made with the subject standing directly or obliquely in front of the tube* or lying supine or obliquely above it. Holzknecht's first oblique position was the one adopted (right shoulder to tube posteriorly, left shoulder to screen anteriorly).

The chief findings may be presented as follows: in general, the bolus is found to reach the cardia in one or two seconds, depending presumably on the amount swallowed and the force employed in the effort. As a rule the food begins to penetrate the cardia in a thin stream without any appreciable delay whatever. In several instances the bolus was held up at the cardia either as a whole or after part had gone through. This was due to causes which cannot be gone into here. In every case examined a bubble of air was seen at the top of the food column (Fig. 1), and in many instances a distinct *niveau* (air above fluid) was in evidence. No peristaltic waves could be made out at any time, the barium column seeming

* By means of the Coolidge tube (Scheidel-Western "Peerless" transformer); practically continuous observations lasting one-half hour or more, were possible.

simply to sink down into the stomach.* In every case in which the second swallowing sound was heard it occurred immediately after

FIG. 1.†—Normal air-swallowing. First oblique position (Holzknecht). Exposure at two seconds after deglutition. Gas present in stomach from previous swallowing. Food column occupies more than half of thoracic esophagus. Narrow stream trickling through cardia. Air bubble above food (no *niveau*).

* On the occasions when a delay occurred at the cardia, there often appeared a rather violent and repeated contraction of the lower part of the esophagus, whereby the *niveau* (when present) was obliterated, the food column narrowed, and the bolus itself propelled for a variable distance up the thoracic esophagus. In such cases, the second swallowing sound was delayed until the spasm was relaxed and the esophagus had expelled its food content. In the most marked instance recorded, the sound was not heard until more than sixty seconds after the original deglutition.

† In taking these plates a rather soft tube was used and exposures were made as short as possible to bring out detail in left diaphragm. The *Magenblase* was generally taken during expiration. Abdominal pressure was avoided so far as possible. The subject was of course always standing, distance of plate from anode being twenty-four inches.

the disappearance of the last portion of food through the cardia. It was, of course, impossible to recognize as such the passage of air into the stomach when this preceded, and in many cases even when this followed, the opaque shadow; but whenever a bubble of air was completely incorporated within the bolus the characteristic sound was heard as it passed the cardiac boundary. In the reclining

FIG. 2.—Normal *Magenblase* before belching. Same individual as Fig. 3.

position, as might be expected, the whole process of deglutition takes longer. The bolus reaches the cardia in from two to four seconds and does not leave the esophagus completely for eight to thirteen seconds. In this case, as a rule, more than one swallowing sound is heard. Very often a murmur occurs at the beginning of cardiac passage in three or four seconds. Next a succession of sounds may appear at intervals as air mixed with the food passes the cardia. Finally, with

the complete disappearance of the bolus, an entire series of squirts may be heard, at times interrupted by acts of inspiration.

It follows from the above observations that the production of swallowing sounds is due chiefly to two factors. The first is the presence of air in the bolus; the second is the force of gravity. In other words, the time of occurrence as well as the number of swallow-

FIG. 3.—Same individual as Fig. 2, after belching. Note: changed position of diaphragm; small amount of residual air in stomach; change in shape of food column (narrower and longer), and small bubble of air at top of duodenal cap.

ing sounds depends entirely upon the position and distribution of the air contained in the bolus. A third factor plays a role of almost equal importance. If the cardia is open when the food arrives it is possible for (some of) the air to precede the bolus, and we then have the first swallowing sound just as Meltzer described it. If the cardia is relatively contracted, as is more often the case, there is time, in

the erect posture, for all the air to rise to the top of the fluid, and then only one—the second—swallowing sound is heard.

Let us now direct our attention to the gastric side of the picture. In the fasting condition, as a rule, no distinct *Magenblase* is dis-

FIG. 4.—Stomach of air-swallower filled with standard barium meal. Note amount of air swallowed with food.

cernible. Only an indefinite light area can be made out in the region of the fornix. With the very first swallow, however, a clearly defined bubble of air appears in the stomach. This, with the opaque food below it, gives the typical roentgen appearance of initial gastric

filling, viz., a light semicircle capping a dark inverted triangle. With each successive swallow the *Magenblase* increases in dimensions. Here an important distinction must be noted. In the hypersthenic or stout members of the group examined, with their high-placed, oblique stomachs, the *Magenblase* became flatter and flatter until it appeared above the horizontal food level as a broad but very shallow segment of a very narrow oval. In these cases the swallowing sound,

FIG. 5.—Same individual as Fig. 4 (air-swallower). Standard barium meal with six additional deglutitions of air. Note thinning and elevation of left diaphragm.

never very loud, became rapidly higher pitched and fainter, until by the time the first glass was consumed (250 c.c.) the murmur was generally inaudible. As soon as belching occurred, which was usually early, the swallowing sound was restored. On the other hand, in the slim, relatively asthenic individuals, with long, narrow, ptotic stomachs, the *Magenblase* reached a larger size, retaining its rounded form, or becoming actually pyramidal, with the apex downward.

The swallowing sound was loud and persisted practically unchanged throughout the entire filling.

So far we have considered what takes place with single swallows of fluid.* When repeated deglutitions are made, as in ordinary

FIG. 6.—"Gas splint." No swallowing sounds. Note accumulation of gas in distal colon compressing stomach. Patient with constipation.

swallowing, relatively less air is admitted into the stomach. The actual amount of gas ingested seems, again, to depend upon the behavior of the cardia. If the latter is relatively patent, a clear space

* It may be of interest to mention that Duroziez[62] used this method—"faire boire le malade a petits coups"—in order to create a zone of resonance against which the lower border of the heart could be percussed out.

(air) can generally be made out between two successive food masses. In this case a swallowing sound is heard after each deglutition. If, as is more commonly the case, the cardiac relaxation is less complete, the food column is added to by each successive swallow until the esophagus is filled almost to its mouth. In this case a relatively small amount of air is admitted, and but a single swallowing sound is heard when all the food has entered the stomach.

One further observation is of importance. If there is a large accumulation of gas in the distal (*i. e.*, terminal part of transverse splenic and descending) colon (Fig. 7) no swallowing sound is heard, at least until after a considerable amount of food is ingested. This finding was particularly marked in patients with constipation and intestinal flatulence. The most reasonable explanation of this phenomenon is that such gas accumulations pad or splint the stomach in such a way as to prevent that degree of vibration necessary for the production of a murmur. That the audibility of the swallowing sounds depends to a definite extent on the tonus of the gastric musculature is borne out not only by the previously described difference between the hypertonic and the subtonic cases, but by the additional fact that in the reclining posture (in which the gastric wall tension is presumably lessened) the most hypertonic cases will present loud and reverberating swallowing sounds.

THE SWALLOWING OF AIR ALONE; "AIR-GULPING." Several observers have described their personal experiences with air-swallowing. Magendie[76] learned the practice himself and taught it to twenty of his students. Weissgerber[94] was the first to publish a detailed account of the mechanism he followed.

The Mechanism of "Air-gulping." The writer taught himself to swallow air by following Weissgerber's directions. In performing an ordinary esophageal eructation—that type of eructation subject entirely to voluntary control—two distinct steps are involved. In the first of these the air normally present in the pharynx is forced for a varying distance into the esophagus. In the second step—which follows immediately after the first—the air is rejected by increasing the intrathoracic and intraesophageal pressure as the result of an act of forced expiration with closed glottis. Both these phenomena are associated externally with a rise and fall of the larynx, a movement which is more rapid and more marked in the first instance, slower and less evident in the second. Two sounds also accompany the act. In the first step, the mouth being closed, the sound is muffled; in the second step, the mouth being generally open and the soft palate vibrating, the sound is correspondingly louder. It is not difficult to learn to dissociate these two phenomena, and ultimately, by suppressing the second, to prevent the escape of air from the esophagus. If now, after executing the first movement, an ordinary "empty" swallow be taken, the air previously forced into the esophagus will be propelled by means of peristalsis

into the stomach. That this is actually the case is shown by the following experiences:

1. Immediately after the swallow a sense of constriction (the degree depending upon the size of the air bolus) was noted in the upper chest, and felt to travel slowly down toward the epigastrium. The feeling is similar to that accompanying the ingestion of too large a piece of food. That the sensation in the latter instance is due to accompanying peristalsis was shown by Hertz[103] in the course of his experiments on sensations in the esophagus.

2. If the epigastrium was auscultated during this experiment a loud murmur was heard two to four seconds after the deglutition. With the appearance of the sound a sense of relief from constriction was experienced.

3. The procedure was repeated, under simultaneous fluoroscopic and auscultatory observation, by one of the subjects of experiment. Coincident with the occurrence of the swallowing sound a large bubble of air was seen to enter the stomach.

4. After repeated deglutitions in the manner described a moderate sensation of distention was experienced. This sensation was relieved after a spontaneous, gastric eructation.

5. Several deglutitions were performed with the mouth and throat full of tobacco smoke. The smoke was not inhaled into the lungs. After an interval, sometimes as long as several minutes, smoke was belched out of the stomach.

It is not absolutely necessary, however, to execute an accessory swallowing movement in order to bring air into the stomach. If the first stage only of an esophageal eructation be executed the air introduced into the top of the esophagus will be propelled downward by the secondary peristalsis so thoroughly investigated by Meltzer,[112 119] Cannon,[96] Quincke[122] and others. Furthermore, if sufficient force be used, and *especially if the cardia be relaxed at the time*, the air may be squirted into the stomach directly, without the intervention of peristalsis, as was originally suggested for the case of fluids, by Kronecker and Meltzer. That this is more than a mere possibility seems evident from the observations made on two of the subjects of experiment, both adepts at air-swallowing. Under simultaneous fluoroscopy and auscultation the air was both seen and heard to enter the stomach within two seconds after the beginning of the act. Moreover, there was no sense of peristalsis experienced by the subjects under these conditions. Indeed, it is by no means unlikely that many of the air-swallowers and belchers met with clinically are cases of (perhaps voluntary) relaxation of the cardia.

In order to describe this mechanism of air entry into the stomach, and to distinguish it from the swallowing of air with food, the term "air-gulping" seems preferable to any other. As already suggested this is, in the writer's opinion, the ordinary maneuver practised by air-swallowers, whether their digestions be healthy or disordered.

However, there has been a tendency among certain writers (Quincke (1889),[88] Pitres (1895),[85] Linossier (1901),[73] Soupault (1906),[90] Cade (1910)[61]) to regard as essential certain respiratory phenomena said to accompany the act of air deglutition. Indeed, the term "air inspiration" has achieved a certain popularity, and graphic studies have been undertaken (Chatin and Tremblay, quoted by Cade[61]) to show the part played by the diaphragm and other muscles of respiration during the process. A description of the act of aerophagia, according to this teaching, is as follows: The subject closes his mouth, lowers his chin and executes a movement of deglutition. This is accompanied or preceded by an inspiratory effort with closed glottis. In this manner the thorax is dilated, an increased negative pressure occurs in the esophagus and the intra-esophageal penetration of a bolus of air is facilitated.

Although the writer has obtained no evidence which would justify him in denying categorically the possibility (at least in certain cases) of "air inspiration," it should be mentioned that in the course of his fluoroscopic observations it was definitely noted that air could be swallowed with the diaphragm in deep expiration just as well as in deep inspiration. Furthermore, it seems quite certain that a simple deglutition ("empty swallow"), unassociated with an actual gulping of air, does not introduce any appreciable amount of gas into the stomach no matter what the intrathoracic pressure relations may be. Now, as it is absolutely essential for the esophagus mouth to be relaxed before anything can pass into the gullet (Killian), some reflex mechanism other than swallowing (which does not introduce air) must be invoked for this purpose. Thus, to be sure, it is conceivable that an inhibition with gaping of the esophagus, such as Killian has observed in gagging or retching, may take place. So far, however, no work has been done with this possibility in mind, and it seems therefore best to regard the case for "air inspiration" as not yet proved.

Experimental. Two of the ten subjects examined were skilful air-swallowers. It was found that but five or six gulps were sufficient to distend the fornix and tubus of the empty stomach, and in some cases, though much less fully, the pyloric vestibule as well. The left diaphragm was raised considerably to a point about 2 or 3 cm. above the level of the right. The gulping of air into the filled stomach not only raised the diaphragm but caused a depression of the food level as well, with an associated broadening of the stomach through the tubus (Fig. 5).

In some cases, as already mentioned, air would penetrate the stomach practically at once after the gulp. Here a wide relaxation of the cardia was assumed. Where the passage took longer the aid of peristalsis was invoked. It was found that although the peristalsis was associated with a sense of constriction in the standing posture this sensation was absent reclining, even when the air did not

enter the stomach for as long as three seconds. In general, also, it was much easier to swallow air in the recumbent than in the standing position.

IV. THE FATE OF AIR IN THE STOMACH.

BELCHING. The greater part of the air introduced into the stomach escapes through the esophagus by eructation. This act has been shown by v. Mikulicz[120] and others to be a true reflex, and necessitates an inhibition of the normal tonic contraction of the cardia.* The factors bringing about this inhibition are many and interesting, and have been the subject of much investigation.

Intragastric Pressure. Kelling[69] has found that belching occurs whenever intragastric tension reaches 25 cm. of water. Under ordinary conditions of swallowing the receptive relaxation of the stomach (Cannon) provides for a *fall* in intragastric pressure. What then are the factors which may occasion such a rise as that found by Kelling? In the first place it is generally agreed that the pressure within the stomach increases as digestion progresses (Dobrovici),[62] and it is quite possible that during the contractions associated with active peristalsis some gas may be forced through the cardia. Furthermore, it should be borne in mind that a bolus of air differs from a solid or fluid bolus in that it increases in size after its introduction into the stomach owing to the difference in temperature between the atmosphere and the interior of the body. A simple calculation shows that whereas outside air swallowed in summer (80° F.) would increase by 4 per cent. of its volume, the same amount of air swallowed in winter (40° F.) would increase by 12 per cent. of its volume.

Gastric Hyperesthesia. It has already been suggested that in individuals with hypertonic stomachs, belching of air swallowed with food occurs earlier than in those with more lax gastric musculature. This is the general rule, and is the common experience in examining patients by means of the fluoroscope. That the question is not entirely one of gastric tonus, however, was suggested by the reactions of the two air-swallowers in the series examined by the writer. Both of these individuals were of the slim build, with long stomachs reaching below the level of the iliac crests. Whereas one of the subjects could store relatively large quantities of air in his stomach with little distress and for long periods, the other, who incidently presented the greater ptosis, was so inconvenienced by the presence of air in his stomach that he was forced to belch after every five or six deglutitions. We may speak of this individual as being hypersensitive to gas. In the experimental

* It is extremely likely that there is an inhibition of the esophagus mouth as well. Killian,[105] who has observed this to occur in vomiting, mentions nothing of the behavior of this sphincter during eructation.

study undertaken by Dobrovici, it was found that in a series of 18 air-swallowers the greater number (13) showed this peculiar hyperesthesia of the stomach to distention, whereas the other 5 could stand an intragastric pressure of 20 to 25 cm. without much discomfort.

Posture. Belching is aided by the erect posture or by lying on the left side. The act is difficult or impossible in the right lateral, the prone, the supine or the inverted postures.

Acidity. Cannon described the acid closure of the cardia.[96] At the beginning of digestion this sphincter showed frequent relaxation with regurgitation of stomach contents. As the acidity rose, these regurgitations ceased. These findings in animals were confirmed by the following personal experience. Some air was swallowed and then about 15 c.c. of $\frac{N}{10}$ HCl was ingested. The usual eructation did not take place: the gas had been effectually sealed in the stomach. However, soon after a corresponding amount of alkali (NaOH) was taken the air began to make its way out through the esophagus.

Peripheral Reflexes. It is an old clinical observation that the stimulation of certain distant parts of the body, particularly in "neurotic" individuals, may provoke eructations. Thus, Frank (1842)[66] reports this effect from the pressure of the forearm in an old man, from feeling the pulse in a woman, from the movements of the waltz in a young girl. Mathieu and Follet,[77] Bouveret,[59] Leven,[71] Soupault[90] have reported similar observations. In addition to seeing such an instance of "eructogenic zone" at the epigastrium the writer had the opportunity of observing a very interesting phenomenon in a woman with a sinus leading to the liver. When barium paste was injected beyond a certain amount the patient was seized with a desire to eructate. We have here a rather striking analogy to the clinical association of belching with affections of the biliary passages.

Belching and Aerophagia. As already indicated, esophageal differs from gastric belching in that the former is voluntary, whereas the latter is not. The esophageal belch is further to be distinguished from the other by the characteristic that it is a double phenomenon in which the gulping down of air precedes its expulsion from the gullet. Individuals subject to flatulence have used this voluntary esophageal belching as a means of provoking spontaneous gastric eructations. By what mechanism is this accomplished? To be sure, it is conceivable that the expulsive effort (constituting the second step of the artificial eructation) may be performed just at the moment when the cardia is relaxed by the gulp, in which case the gastric gases should be expelled summarily. As will be shown presently it takes but a very few eructations to evacuate even large gas accumulations. That this does not take place in the case under discussion is strongly suggested by the fact that these

efforts are repeated again and again by the patient. What is indeed much more likely is that the second step of the eructation not only fails to remove all the air from the esophagus, but that the residue is really carried into the stomach. Mathieu,[78] who auscultated these cases, actually heard the gurgle accompanying the passage of air through the cardia, a finding which the writer has confirmed on more than one occasion. In this way the patient (unintentionally, of course) introduces additional air with each successive "eructation," until the intragastric tension becomes so great that spontaneous gastric belching occurs and brings relief. It is for this reason that all persistent belchers should be regarded clinically as air-swallowers.

Inhibition. In the course of our experiments it was found that one of the subjects could inhibit an impending spontaneous eructation by swallowing more air or by executing a simple deglutition. In this case it may be assumed that the intragastric tension was depressed as described by Cannon. That the discharge of the deglutition reflex is associated with a general inhibitory effect was one of the earliest observations published by Meltzer.[111 115]

Experimental. The two air-swallowers were fluoroscoped while trying to assist or provoke gastric eructations. The diaphragm was depressed to the limit, the abdominal wall was pulled in, and the intra-abdominal pressure was further increased by flexing the thighs on the abdomen and bending the trunk forward. When these manipulations were successful the middle field (space between the heart and the spine in the oblique position) would light up brightly, indicating the passage of a large amount of air up the esophagus. At the same time the characteristic sound would be heard and the *Magenblase* would practically disappear, the food level rising, and the left diaphragm descending, to its normal position. As a result of these changes the entire stomach becomes shorter and narrower than before, whereas the food column itself becomes correspondingly longer. Even the largest gas accumulation is almost entirely evacuated after five or six belches, while the ordinary *Magenblase* noted after the ingestion of a standard opaque meal is generally brought up in a single eructation (Figs. 2, 3 and 4).

PASSAGE INTO THE INTESTINE. When air is swallowed with food in the erect position there is very little opportunity for the former to go through the pylorus. As already mentioned, by far the greater part is belched up long before the rest of the stomach contents are evacuated. In the reclining position the entrance to the pylorus seems more accessible.

On the other hand, if air is swallowed on an empty stomach, the gas may make its escape through both outlets. The following fluoroscopic observations were made on one of the air-swallowers. Six gulps of air were taken on an empty stomach within a period

of thirteen minutes. One-half minute after the last deglutition a loud gurgle was heard over the pylorus (Meltzer's *Pylorusgeräusch*).[117] This was associated with some relief in the sensation of distention and with the appearance of light areas below and to the left of the stomach (gas in the small intestine). Following this a few eructations and a greater number of pyloric passages were recorded. The latter were aided by deep inspirations or by bending forward. Certain loud gurgles, which were unaccompanied by a change in the sense of gastric tension, were ascribed to small intestinal peristalsis. The stomach was practically empty in forty-five minutes.

Absorption by the Mucosa. That oxygen is readily absorbed by the gastric mucosa is an old observation (see work of Planer and Giglio mentioned above). Recent studies have shown that the rate of this absorption is approximately 12 c.c. per minute (Yllpö).[54] It is therefore probable that whatever gas is passed into the small intestine at the end of an ordinary period of digestion consists chiefly of nitrogen with some CO_2 from the stomach. In the fasting stomach, however, whole air may pass through the pylorus. Yllpö reports that he experienced considerable flatulence two to four hours after the ingestion of air under these conditions, whereas the taking of large amounts of CO_2 and of O was not followed by this sensation. The difference, of course, is due to the unabsorbed nitrogen present in the first instance.

V. SUMMARY.

1. In general, gaseous accumulations in the upper digestive tract have atmospheric air as their basis.

2. This air is introduced by ordinary swallowing or by an adaptation of the swallowing mechanism known as gulping.

3. The differences between the swallowing of air and that of food depend to a large extent on the influence of gravity. As a result the swallowing mechanism shows certain peculiarities which are described in this paper.

4. By means of fluoroscopic observations it can be demonstrated that the so-called swallowing sounds are produced by the entry of air into the stomach.

5. A close study of the mechanism of deglutition based upon a review of the literature and on original roentgen-ray observations shows the advantage of describing the complete act of swallowing as consisting of three instead of the classic two periods. These three periods are the buccopharyngeal, the esophageal and the cardiogastric.

BIBLIOGRAPHY.

(NOTE.—The asterisked (*) references have not been verified.)

A. GASES OF THE STOMACH AND INTESTINE. GENERAL LITERATURE.

1. Andral, G.: Cours de pathologie interne, Paris, 1848, 2ed., i, 124.
2. Bardet: Bull. et mém. de la soc. de méd. et de chir. prat. de Paris, 1894, 122–3.
3. Basch, S.: New York Med. Jour., 1908, lxxxviii, 684; 738.
4. Baumes, P.: Lettres sur les causes et les effets de la présence des gaz ou vents dans les voies digestives, Paris, 1832, 1833 (Seven letters).
5. Benedict, A. L.: Internat. Clinics, 1899, iii (9 ser.), 149.
6. Boas, J.: Deutsch. med. Wchnschr., 1892, xviii, 1110–1112.
7. Carius: Quoted in extenso in Schultze.[48]
8. Chevillot, P. F.: Thèse, Paris, 1833; repub. in Gaz. méd. de Paris, 1833, i, 617.
9. Chomel: Art. Pneumatose, in Dictionnaire de médecine, Paris, 1842, 128.
10. Chomel: Des dyspepsies, Paris, 1857, 87.
11. Combalusier: Pneumo-pathologia seu tractatus de flatulentis humani corporis affectibus, Paris, 1747.
12. Dallemagne, J.: Arch. de méd. exp., 1895, vii, 274.
13. Eichorst: Handbuch der speziellen Pathologie u. Therapie, Wien, 1887, 2, 3ed., 168.
14. Emminghaus: Berl. klin. Wchnschr., 1872, ix, 477; 491.
15. Ewald, C. A.: Arch. f. Anat., Physiol. u. wiss. Med., 1874, 217.
16. Ewald, C. A.: Deutsch. med. Wchnschr., 1910, xxxvi, 641.
17. Gerardin: Thèse, Paris, 1814.
18. Giglio, C.: Gazz. Sic. di Med. e. Chir., 1905, iv, 561; 577.
19. Van Helmont, J. B.: De Flatibus, in Ortus Medicinæ, Amsterdam, 1648, 413.
20. Heynsius, A.: Tijd. voor Geneesk., 1874, i, 561.
21. Hippocrates: Des vents, in Oevres complètes d'Hippocrate (Tr. Littré), Paris, 1849, vi, 88.
22. Hoppe-Seyler, G.: Deutsch. Arch. f. klin. Med., 1892, l, 82.
23. Hoppe-Seyler, G.: Verh. d. Kong. f. inn. Med., 1896, xiv, 561.
24. Howell, W. H.: A Text-book of Physiology, Philadelphia, Saunders, 1908, 2ed., ch. 36.
*25. Jurine: Mém. de la soc. de méd., 1789, x, 77 (quoted by Vauthey).
26. Korach, S.: Deutsch. med. Wchnschr., 1880, vi, 275; 290.
27. Kuhn, F.: Ztschr. f. klin. Med., 1892, xxi, 572.
28. Kuhn, F.: Deutsch. med. Wchnschr., 1892, xviii, 1107; 1140.
*29. Lameyran and Fremy: Bull. de Pharm., 1819, i, 358 (quoted by Giglio).
30. Luton, A.: Dyspepsie, in Nouveau Dictionnaire de médecine et de chirurgie Pratiques, Paris, 1870, xii, 59.
31. Luton, A.: Tympanite, in Nouv. Dict. de Méd., etc., Paris, 1870, xxxvi, 448.
*32. Magendie and Chevreul: Nouv. Bull. de la Soc. Philomatique, 1814, iv, 129 (quoted by Ewald, Giglio, etc.).
33. McNaught, J.: Med. Chron., 1893–4, xix, 73.
34. Miller: Deutsch. med. Wchnschr., 1885, xi, 843.
35. Miller: Deutsch. med. Wchnschr., 1886, xii, 117.
36. Mills: Ann. de la soc. roy. des sci. méd. et nat. de Bruxelles, 1896, v, 265.
*37. Minkowski: Mitt. a. d. med. Klin. zu Königsberg, 1888 (quoted by Vauthey).
38. Moreau, A.: Ann. des sci. nat., 1876, iv (6 ser.), 80.
39. Naunyn, B.: Deutsch. Arch. f. klin. Med., 1882, xxxi, 225.
*40. Planer: Sitzungsber. der Wien. Akad. der Wissens., 1860, xlii, 307 (quoted by Hoppe-Seyler, Giglio).
*41. Poensgen: Dissert., Strassburg, 1879 (quoted by Vauthey).
42. Popoff, L.: Berl. klin. Wchnschr., 1870, vii, 453; 466; 477.
43. Popoff, L.: Arch. f. d. ges. Physiol., 1875, x, 113.
44. Riegel: Deutsch. med. Wchnschr., 1892, xviii, 467.
45. Schierbeck, N. P.: Skand. Arch. f. Physiol., 1892, iii, 437.
46. Schierbeck, N. P.: Skand. Arch. f. Physiol., 1895, v, 1.
47. Schultze: Berl. klin. Wchnschr., 1874, xi, 317, 336.

48. Strauss, H.: Ztschr. f. klin. Med., 1894, xxvi, 514.
49. Strauss, H.: Berl. klin. Wchnschr., 1896, xxxiii, 385.
50. Tappeiner, H.: Ztschr. f. physiol. Chem., 1882, vi, 432.
*51. Vauquelin: Mém. du musée, 1817, iii, 279 (quoted by Giglio).
52. Vauthey, P.: Thèse, Lyon, 1896.
53. Woodyatt, R. T., and Graham, E. A.: Ohio State Med. Jour., 1912, viii, 407.
54. Yllpö, A.: München. med. Wchnschr., 1916, lxiii, 1650.
55. Yllpö, A.: Detailed account of preceding to appear in Biochem. Ztschr. (announced in [54]).

B. Air-swallowing. Eructation.

56. Abrams, A.: Philadelphia Med. Jour., 1899, iv, 315.
57. Aubert, P.: Lyon médicale, 1891, lxvii, 510, 547.
57 bis. Barclay, A. E.: The Stomach and Oesophagus, London, Macmillan, 1913.
58. Bouveret, L.: Rev. de méd., 1891, xi, 148.
59. Bouveret, L.: Lyon médicale, 1901, xcvi, 349.
60. Bouchholz, E.: Thèse, Paris, 1913.
61. Cade, A.: Précis des maladies de l'estomac (Collection Testut), Paris, 1910, 277.
62. Dobrovici, A.: Thèse, Paris, 1906.
63. Duroziez: Traité clinique des maladies du coeur, Paris, 1891.
64. Eisler, F., and Kreutzfuchs, S.: Wien. med. Wchnschr., 1912, lxii, 2951.
65. Falke, J. E. L.: Arch. f. path. Anat., 1863, xxvi, 38.
66. Frank, J. P.: Traité de médecine pratique (tr. from Latin by Goudareau), Paris, 1842, ii, 12.
67. Heusinger, C. F.: Arch. f. path. Anat., 1862, xxiv, 286.
68. Hoffmann, F. A.: München. med. Wchnschr., 1905, lii, 832, 1177.
69. Kelling: Arch. f. klin. Med., 1901, lxiv, 393 (see p. 403).
70. Lesage, Leven, and Barret: Comp. rend. hebd. des séances et mém. de la Soc. de biol., 1908, lxv, 471.
71. Leven, G.: L'aérophagie, in La Dyspepsie, Paris, Doin, ch. 4, 115.
72. Leven, G., and Barret, G.: Radioscopie gastrique et maladies de l'estomac, Paris, Doin, 1909.
73. Linossier: Bull. et mém. de la Soc. méd. des hôp. de Paris, 1901, xviii (3 ser.), 209.
74. Lyon, G.: Diagnosic et traitement des maladies de l'estomac, Paris, 1909.
75. Lyonnet and Vincens: Lyon méd., 1901, xcvi, 189.
76. Magendie, F.: Mémoire sur la deglutition de l'air atmosphérique, Paris, 1813.
77. Mathieu, A., and Follet, R.: Bull. et mém. de la Soc. méd. des hôp. de Paris, 1901, xviii (3 ser.), 199.
78. Mathieu, A.: Gaz. des hôp., 1904, lxxvii, 23 (also in German, Arch. f. Verdauungsk., 1904, x, 29).
79. Morange, G.: Thèse, Paris, 1903.
80. Obici, G.: Atti della accad. delle scienze med. e nat. in Ferrara, 1895, lxix, 131.
81. Perrody, A.: Thèse, Paris, 1902.
82. Pierquin: Jour. gén. de méd., chir. et pharm., 1830, iii, 319.
83. Piorry: Bull. de l'Acad. de méd., 1871, xxxvi, 943, 953.
84. Pitres, A.: Le progrès méd., 1895, i (3 ser.), 17.
85. Quincke, H.: Verh. des Kong. f. inn. Med., 1889, viii, 377.
86. Rosenbach, O.: Wien. med. Presse, 1889, xxx, 552, 600.
87. Smith, C. H., and Le Wald, L. T.: Am. Jour. Dis. Child., 1915, ix, 261.
88. Spivak, C. D.: Med. Rec., 1905, lxvii, 649.
89. Soupault, M.: Bull. et mém. de la Soc. méd. des hôp., 1901, xviii (3 ser.), 221.
90. Soupault, M.: Traité des Maladies de l'Estomac, Paris, Baillière, 1906, 210.
91. Thomas, J.: Thèse, Paris, 1912.
92. Variot: Bull. et mém. de la Soc méd. des hôp. de Paris, 1901, xviii (3 ser.), 230.
93. Vincens: Thèse, Lyon, 1900.
94. Weissgerber, O.: Berl. klin. Wchnschr., 1878, xv, 521.

C. The Mechanism of Deglutition. Swallowing Sounds.

95. Allbutt, T. C.: British Med. Jour., 1875, ii, 420.
96. Cannon, W. B.: The Mechanical Factors of Digestion, London, Arnold, 1911.
97. Cannon, W. B., and Lieb, C. W.: Am. Jour. Physiol., 1911, xxvii, p. xiii; 1911, xxix, 267.
98. Cannon, W. B., and Moser, A.: Am. Jour. Physiol., 1898, i, 435.
99. Eykman, P. H.: Arch. f. d. ges. Physiol., 1903, xcix, 513.
100. Hamburger, W.: Med. Jahrbücher, 1868, xv, 133.
101. Held, I. W., and Gross, M. H.: Jour. Am. Med. Assn., 1916, lxvi, 233.
102. Hertz, A. F.: British Med. Jour., 1908, i, 130; also Guy's Hosp. Rep., 1907, lxi, 389.
103. Hertz, A. F.: The Sensibility of the Alimentary Canal, London, Frowde, 1911, 17.
104. Hirsch, I. S.: Interstate Med. Jour., 1916, xxiii, 42.
105. Killian, G.: Ztschr. f. Ohrenh. u. f. Krankh. d. Luftwege, 1908, lv, 1.
106. Kindermann, J. C.: Nederl. Tijdschr. voor Geneeskunde, 1903, xxxix (pt. 2), 1182.
107. Kraus, F.: Ztschr. f. exp. Path. u. Ther., 1912, x, 393.
108. Kraus and Ridder: Die Erkrankungen der Mundhöhle, u. der Speiseröhre, Vienna, Hölder, 1913, 2d ed., ii.
109. Kronecker and Falk: Arch. f. (Anat. u.) Physiol., 1880, 296.
110. Kronecker, H., and Meltzer, S. J.: Arch. f. (Anat. u.) Physiol., 1880, 446.
111. Kronecker, H., and Meltzer, S. J.: Proc. Roy. Soc., London, 1881–2, xxxiii, 27.
112. Kronecker, H., and Meltzer, S. J.: Arch. f. (Anat. u.) Physiol., Ergzgsbd., 1883, 328.
113. Magendie, F.: Mémoire sur l'esophage, Paris, 1813.
114. Magendie, F.: Précis élémentaire de physiologie, Paris, 1817, ii, 58.
115. Meltzer, S. J.: Arch. f. (Anat. u.) Physiol., 1883, 209.
116. Meltzer, S. J.: Centrabl. f. d. med. Wiss., 1883, xxi, 1.
117. Meltzer, S. J.: Berl. klin. Wchnschr., 1884, xxi, 447, 462.
118. Meltzer, S. J.: Jour. Exp. Med., 1897, ii, 453.
119. Meltzer, S. J.: Proc. Soc. Exp. Biol. and Med., 1906–7, iv, 35.
120. v. Mikulicz, J.: Mitt. a. d. Grenzg. d. Med. u. Chir., 1903, xii, 569.
121. Müller, A., and Saxl, P.: Wien. klin. Wchnschr., 1908, xxi, 483.
122. Natanson, L.: Centralbl. f. d. med. Wiss., 1864, ii, 833.
123. Quincke, H.: Arch. f. exp. Path. u. Pharm., 1886–7, xxii, 385.
124. Scheier, M.: Beitr. z. Anat., Physiol., Path. u. Ther. des Ohres, der Nase u. des Halses, 1910–11, iv, 115.
125. Schlippe, P.: Deusche. Arch. f. klin. Med., 1903, lxxvi, 450.
126. Schreiber, J.: Arch. f. exp. Path. u. Pharm., 1901, xlvi, 414.
127. Schreiber, J.: Arch. f. Verdauungsk., 1911, xvii, 647.
128. Schreiber, J.: Arch. f. exp. Path. u. Pharm., 1911–12, lxvii, 72.
129. Zenker, W.: Allgem. Ztschr. f. Psychiat., 1869, xxvi, 457.
130. Zenker, W.: Berl. klin. Wchnschr., 1884, xxi, 38.

VITAL STAINS AND THE CENTRAL NERVOUS SYSTEM.

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THE necessity for studies relative to the conveyance of substances to the central nervous system is indicated by the relative inadequacy of the treatment of quaternary syphilis by means of intravenous injections of arsenical preparations.

It has been assumed that substances introduced intravenously do not reach the cerebrospinal fluid or the brain. Failure to reach the cerebrospinal fluid has been accepted as the criterion of failure to reach the brain. This assumption has been reached through such investigations as have shown that arsenic, mercury and antimony do not pass the choroid plexus into the cerebrospinal fluid (Mott). Agglutinins of typhoid fever, bacterial toxins and hemolytic amboceptors do not enter the fluid. The explanation for this phenomenon has been sought for in many directions. *Intra vitam* staining of the central nervous system has been one of the principal method of research.

Trypan blue, a benzidine dye, was selected for experimental purposes because of the similarity of its physicochemical properties and its organotropic characteristics to salvarsan. Trypan blue when intravenously injected at first rapidly diffuses and gives an intense general stain to the tissue; finally, however, it is stored up in specific cells, the pyrrhol cells.

Goldmann[1] has shown that after an intravenous injection of trypan-blue solution the brain and cerebrospinal fluid remains unstained. This observation has been confirmed by Frazier, Tilney, Woolsey, Hecht, Evans, one of us and others, and has been already remarked by Bouffard.

This singular action of the central nervous system has been explained in a number of ways.

Goldmann explained it on the basis of the filtering action of the choroid plexus. The fallacy of the conclusion is shown by the work of Bouffard, who found that following an intravenous injection of trypan blue when the brain remained unstained certain other tissues, as the ovaries and testes, likewise remained unstained. This has been confirmed by one of us (L. J. P.), by Evans, Schuleman and others. It has been found that the parenchyma of the testicle, the

[1] Arch. f. klin. Chir., 1913, ci, No. 3.

cortex of the suprarenal body, portions of the ovaries, the lungs and the brain remain unstained. Only certain cells, the pyrrhol cells, store up this stain, and other cells, as the epithelium of the convoluted tubules of the kidney, are free from stain, as are the blood cells.

It has been known from the work of Ehrlich, Heidenhain and Bethe, and lately has been shown by one of us (L. J. P.),[2] that certain other vital stains, as methylene blue and malachite green, enter into and may be demonstrated in the nervous tissue as well as in other organs following their intravenous administration. Some stains not necessarily of the composition of trypan blue, as fluorescin, cannot be demonstrated in the nervous tissue. Similar observations have been made by McIntosh and Fildes.

They found that with neutral red and alizarin blue the brain was stained, whereas the indigo carmine, light green, acid fuchsin, trypan red and blue and pyrrhol blue it was not. This difference in staining reaction of vital dyes could be due either to failure of the dye to reach certain tissues by reason of structural differences in the bloodvessels or, having reached these tissues, to a variation in the physicochemical reactions between the dye and the tissues.

Recently McIntosh and Fildes[3] argue that certain stains do not penetrate into the brain because the bloodvessels are impermeable to them. They state that the bloodvessels of the brain differ from those in other parts of the body in the possession of an extra-adventitial sheath. Among other conclusions they state that certain dyestuffs can pass directly from the blood to the brain substance without being found in the cerebrospinal fluid, and the inefficiency of certain dyestuffs in passing through the bloodvessels has nothing to do with their absence from the cerebrospinal fluid. They say that the chief factor which governs the passage of the dyes is their solubility reaction, which is not a general lipoid solubility and corresponds to the solubility in chloroform and in water or perhaps to their partition coefficient in these liquids. MacCurdy[4] concluded that vital stains (trypan blue) must penetrate the vessel walls, albeit slowly.

Obviously, permeability of the bloodvessels determines only the capacity of a stain to come into contact with cells, and the degree of penetration into the cell is dependent upon other factors: (1) the permeability of the cell membrane; (2) the reaction of the cell contents to the stain as to solubility, partition coefficient, certain chemical relations of the fats and proteins within the cell and probably other factors.

If the absence of salvarsan from the central nervous system following an intravenous injection could be explained upon the same

[2] Proceedings of the Chicago Pathological Society, 1916.
[3] Brain, 1916, xxxix, 478.
[4] Psychiatric Bulletin, January, 1917, ii, No. 1.

basis as the absence of trypan blue under similar circumstances it must be due to a similar number of factors. McIntosh and Fildes[5] examined the brain of an infant dying after an intravenous salvarsan injection and found no arsenic present. Ullman, Morel and Mouriquad had similar experiences. They all concluded that salvarsan was not neurotropic, and Ehrlich accepted this opinion and concluded that salvarsan had no "Vorliebe" for the brain.

Having shaken 0.15 gm. of neosalvarsan with 100 gm. of minced brain, McIntosh and Fildes were unable to obtain that amount from a number of subsequent washings, and they concluded that their former opinion was wrong and that the brain fixed considerable neosalvarsan.

The fact that minced brain fixed a certain amount of neosalvarsan does not prove that living brain tissue would combine with it. In the latter case we are dealing not only with a mass of inert proteins, lipoids, salts, etc., but with living cells which, because of that very state, bind certain substances together, which in the combined state may refuse to take up matter for which they may have an affinity separately. A number of other factors must also be considered.

There are certain characteristics of vital stains in general and certain laws governing their action which, when reviewed, offer considerable assistance in the explanation of the absence of vital staining of the central nervous tissue with certain dyes.

Overton[6] in a study of vital stains found that stains possessing this property, as neutral red, methylene blue, thionin, etc., in contrast to the sulphonic acid dyes, as water-soluble indulin, nigrosin, anilin blue, etc., were soluble in oils, fats and fatty acids and readily soluble in lipoids, as lecithin, cholesterin, protagon and cerebrin. Furthermore, crumbs of these substances absorbed these vital stains from dilute solutions. He therefore concluded that the cell wall, probably consisting chiefly of lipoids, prevented the penetration of such substances as were insoluble in these lipoids.

Evans and Schuleman[7] point out the fact that although vital stains, the benzidine dyes are insoluble in fats or lipoids, and that the majority of the cells of the body are not surrounded by fat. They state that the diffusion power of a stain affects it merely by enabling the dye molecules to present themselves to the class of cells which will receive them. Having arrived at the cell the benzidine dye by no means diffuses into it, as is the case with various basic dyes (neutral red, methylene blue, etc.). The benzidine dyes filter in more slowly and never encounter physical conditions which favor their rapid spread.

Kite[8] holds that Overton's conclusion that the lipoids are solely

[5] Proceedings of the Royal Society, 1914, B. 88, p. 320.
[6] Jahrb. f. Wissenschaftl. Botanik, 1900, xxxiv, 669.
[7] Science, March, 1914, xxxix, No. 1003.
[8] Am. Jour. Physiol., 1915, xxxvii.

responsible for the solution of vital stains is untenable. Thionin is insoluble in olive-oil benzol and olive-oil lecithin, but is quite soluble in benzol lecithin; if lecithin were the only factor involved the thionin should go into solution with olive-oil lecithin. He conducted a number of experiments with the eggs of marine animals and many plant cells and root hairs. He found that many acid dyes penetrated various cells. Trypan blue and red, anilin blue and nigrosin penetrate many eggs, and isamin blue, indigo carmin and many other stains penetrate plant cells. The eggs of asterias, unstained by certain dyes, trypan blue and red, were punctured and fluidity gradients formed for the purpose of determining whether the plasma membrane theory were correct. If so a dye which penetrates the surface of a swollen area of cytoplasm ought to penetrate the whole interior of the egg. In the majority of cases the dye did not penetrate the surface of the swollen protoplasm. In no case was the whole interior of the egg stained. Puncture of the cell wall or cell wall and protoplast made most of the plant cells permeable to all the common acid dyes which under the same conditions do not penetrate the unpunctured cells, showing that neither the plasma membrane nor the protoplast but the cell wall is responsible for the impermeability of many plant cells for acid dyes.

In an effort to determine further data relative to the possible relations between the diffusion characteristics of dyes, their solubility in certain substances and their vital staining properties, we performed a large number of experiments. These dyes were studied relative to their diffusion through an animal membrane into water and into various organs which were minced and into which a dialyzing tube containing the solution of the stain was embedded. Their staining reaction in very dilute solutions upon minute particles of various tissues was noted; the permeability of yolk and egg membranes to these dyes was observed and solubility of these dyes in fresh brain tissue tested.

Methylene blue penetrated an animal membrane easily into water, brain and muscle tissue. Minute particles of brain, liver and lung are readily stained in very dilute solutions. It penetrated the membrane of the yolk of a hen's egg readily. The yolk was readily stained. Methylene blue when triturated with the brain of a recently dead fetus apparently was soluble in this tissue.

Trypan blue penetrated an animal membrane hardly at all and very slowly into water—at times not at all into brain tissue, at other times to a degree smaller than into water. It penetrated the yolk membrane but did not stain the yolk. It was insoluble in the brain of a recently dead fetus. Minute particles of brain were unstained in very dilute solutions.

Fluorescin penetrated an animal membrane into water more readily than any of the stains investigated. On one occasion when

employing the brain of a recently dead fetus it did not penetrate into the tissue. Upon all other occasions it did. Minute particles of brain were unstained in very dilute solutions. It penetrated yolk membrane readily, but apparently did not stain the yolk.

Nigrosin and anilin blue penetrated an animal membrane into water readily, but they did not penetrate the membrane of an egg yolk.

Diarsenol penetrated the membrane of an egg yolk.

Such stains as penetrated an animal membrane of a dialyzing tube also penetrated the egg membrane.

From a review of the literature cited above and a study of our experiments certain comments may be made.

Vital stains may possess the characteristic of both crystalloids and colloids. Some vital stains stained all tissues alike. This was especially true of stains possessing great diffusibility, such as methylene blue, etc. However, stains showing a similar degree of diffusibility, as fluorescin, left certain tissues unstained. As a rule the benzidine dyes, possessing colloidal properties, had a selective action, and certain tissues were unstained by them.

If the degree of permeability of certain tissues to stains is solely responsible for the vital staining of organs the bloodvessels and the cell membrane must both be permeated. If we assume that the bloodvessels are responsible in preventing such stains as trypan blue from reaching the brain the theory that their impermeability is dependent upon their lipoid character is untenable, because it would have to be assumed that the bloodvessels of the brain possess a different chemical composition from the bloodvessels of other parts of the body. An extra layer of tissue of similar composition, as an extra-adventitial sheath, would not suffice to prevent the escape of the dye if the permeability were governed by physico-chemical laws. The colloid character of dye is probably responsible for failure in penetrating bloodvessels. However, if the colloid character of the dye were solely responsible for its impermeability into the brain, fluorescin should stain the brain easily, which it does not. The experiments of Kite conclusively show that the cell membrane alone is not responsible for absence of *intra vitam* staining. But if it is assumed that the cell membrane is partly responsible for the impermeability of the dye the lipoid character of this membrane does not offer a satisfactory explanation for this phenomenon. It would have to be assumed that the cell membranes of the brain, lung and certain other parts of the body differ in composition from the cell membranes elsewhere. The same objections to this view are valid here as they are when applied to vital stains in general. According to this theory the benzidine dyes which are insoluble in fats or lipoids should not stain any tissue *intra vitam*, which is not the case. On the other hand, Salant and Benges[9] found that

[9] Jour. Biol. Chem., November, 1916, No. 2, xxvii, 403.

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fat-soluble stains when intravenously introduced were deposited chiefly in the adipose tissue. Only occasionally and under certain circumstances, as starvation, was the nervous system stained. The nerves were stained more frequently than the central nervous system.

Therefore the factors entering into the absence of vital staining of any organ are: Impermeability of the bloodvessel for which the colloid character of the substance may be largely responsible; impermeability of the cell membrane where the lipoid character of such a membrane may play some part and the refusal of the cell content to take up the stain.

Trypan blue probably does not penetrate bloodvessels with the ease and rapidity of methylene blue. It does penetrate bloodvessels, and we cannot assume that the bloodvessels of the brain, lung, portions of the testicle, etc., possess different chemical characteristics from those in other portions of the body. It is a vital stain and penetrates cell membrane, the penetrability not being dependent upon solubility in fats or lipoids. Certain cells refuse to combine with this stain in the living state.

When introduced subdurally in sublethal doses it has been found that the meninges are well stained with trypan blue, and the cord and brain, with which the stain has come in contact, is stained to only a slight depth. When introduced in the lumbar region the stain does not extend over the cerebral hemispheres. When introduced intracranially frequently the opposite side has not been reached by the stain. Woolsey[10] has found that, following sublethal doses introduced subdurally, that the meninges in some areas of the brain were not more stained than by intravenous injections. The brain was not sufficiently stained to be visible microscopically, but the cord was stained from a depth of from 0.5 to 1 mm. True nerve cells were infrequently stained with sublethal doses. Although the brain and spinal cord were stained more readily by subdural than by intravenous administration of trypan blue a study of Woolsey's results did not convince one that the portion of the brain and cord stained were stained *intra vitam* and were uninjured. On the contrary, Woolsey was unable to find any great number of real nerve cells that had taken the stain with sublethal doses. The experiments employing the subdural administration of trypan blue were performed with solutions of a much greater concentration (0.1 to 2 per cent.) than salvarsan solutions used therapeutically.

We have performed experiments on fifteen rabbits and six dogs. We employed subdural injections of dilute solutions of trypan blue and fluorescin, ranging from 0.0025 per cent. to 0.1 per cent. From these experiments it may be stated that trypan blue and fluorescin solutions act similarly under these conditions. Solutions of con-

[10] Jour. Nerv. and Ment. Dis., 1915, lxii, 478.

centration not exceeding that employed in the therapeutic injection of salvarsan subdurally did not stain the brain or spinal cord. Perfusion of trypan-blue solution twice this concentration subdurally over one cerebral hemisphere, allowing the exudate to escape in the lumbar region for a period of an hour, stained the brain a slight sky-blue tint, usually on the side of injection, to a depth which could be removed when the brain was wiped with a bit of wet cotton. With 0.1 per cent. solutions introduced subdurally over one hemisphere the brain substance stained very superficially and faintly on the side of injection over a small area of the occipital lobe, chiefly along the bloodvessels and sulci. Both quadrigeminal bodies, the cruræ and the sulci lodging bloodvessels in the cerebellum chiefly on the tentorial side, were superficially stained. The medulla was faintly tinged, the cord was unstained except perhaps in the cervical region, where the stain was hardly perceptible. The meninges of the cord and brain were well stained, except over the side opposite the injection, where the stain was distributed irregularly over the cortex. When the dye was introduced subdurally in the lumbar region, unless injected in large quantities and with enormous force, the cerebral hemispheres were unstained.

Five animals were perfused intravenously with solutions from 0.0025 per cent. to 0.05 per cent., at the same time being bled from the femoral artery. These animals died from five to ten minutes after the blood seemed to have entirely disappeared from the vessel and the muscles were colorless. Under these circumstances the animals injected with 0.05 per cent. showed in the brain a definite change in color, but so slight as to be undefinable. An animal receiving 70 c.c. of a 1 per cent. solution of trypan blue without being bled showed a similar color change in the brain. One animal in which one carotid artery was tied was injected through the opposite carotid with 50 c.c. of 1 per cent. solution of trypan blue. At the end of the time occupied with the injection (five minutes) the animal died. The brain was stained a distinct oyster blue.

Although a slight blue color may be observed macroscopically in cases injected subdurally, microscopic examination has failed to show the presence of a true vital stain. MacCurdy[11] repeated the experiments of Goldmann and found the stain to be an artefact, due to the staining of the fixed tissue by the dye present in considerable concentration.

Although it cannot be proved that such parts of the brain as stain following a subdural injection have changed in viability, it must be assumed that such is the case because the bloodvessels themselves cannot, for the reasons stated above, prevent the penetration of this stain. A substance circulating within bloodvessels through tissues which have no chemical or physical attraction for these substances may be removed too quickly to afford them an

[11] Loc. cit.

opportunity of changing the cell chemistry so that they may penetrate the cell. When applied to these cells in a manner which prevents their rapid removal the cells may undergo a change which permits of their penetration. Any procedure which increases metabolic activity of cells ensures a greater degree of *intra vitam* staining with trypan blue. Whether such an increase, with its attending cell injury as would result from the introduction subdurally of relatively large doses of the stain, or, analogously speaking, large doses of salvarsan are harmless and beneficial, cannot be stated.

It would seem proper to conclude that when dealing with colloidal stains or drugs the meninges are more accessible by subdural than by intravenous routes. This cannot be stated of the central nervous system. When intravenously introduced, certain dyes and salvarsan fail to reach the central nervous system largely because of the physicochemical reactions between the substance and the tissues. The permeability of the bloodvessels plays but a small role and the cerebrospinal fluid and choroid plexus none at all.

Finally, salvarsan, which probably like trypan blue leaks from bloodvessels relatively slowly, when intravenously introduced possesses as great a spirochetocidal action upon those organisms situated in the pia, adventitia and perivascular lesions in the brain as elsewhere, providing the spirochetes have not developed a peculiar resistance to such a drug.

THE CIRCULATORY REACTIONS TO GRADUATED WORK IN NORMAL PEOPLE AND IN THOSE WITH CARDIAC INSUFFICIENCY.

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NEW YORK.

(From the Second Medical Division of the New York Hospital.)

The important part which physical training plays in the preparation of soldiers for active service and in promoting convalescence from disease or injury makes it desirable to reinvestigate the circulatory reactions following work in both normal people and in those with damaged hearts to see if we can find in these reactions anything which will serve as a guide in estimating the condition of the cardiac reserve power.

We shall first take up the effects of work upon the systolic blood-pressure in normal people. There are two methods of determining the pressure curve after work. In one described by Rapport,[1] readings are taken very frequently (five- to ten-second intervals) by

[1] Arch. Int. Med., 1917, xix, 981.

palpation. In the other method, which we have used for some time, readings are made less frequently by auscultation and at practically equal intervals. Our method is much more convenient, and enables us, as we will shortly show, to construct the curve with sufficient accuracy to achieve our purpose.

For these experiments a sphygmomanometer of the Riva-Rocci type, with a web-covered rubber bulb, was used. The pressure was read by auscultation until it had reached a constant level. The cuff remained on the arm during work and a reservoir of air under pressure was maintained in the rubber bulb. With coöperation on the part of patient and assistant we were generally able to make the first reading, when so desired, as soon as ten seconds had elapsed, and at short intervals thereafter. When using our own method[2] of infrequent readings we made the first reading between twenty-five and thirty seconds after work; the second between fifty-five and sixty; the third between eighty-five and ninety. We endeavored to make the readings as close to thirty, sixty and ninety seconds as was possible.

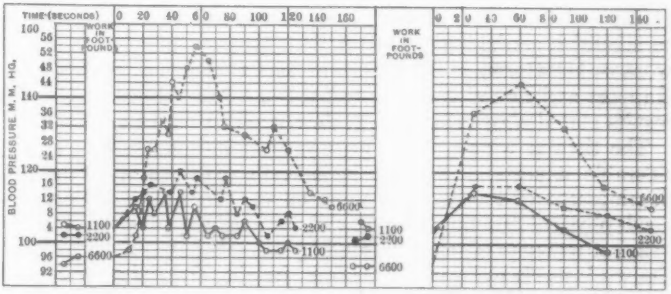

CHART I.—Blood-pressure reactions in a normal man after increasing amounts of work furnished by swinging dumb-bells. Five to ten minutes intervened between the individual exercises. In this and in the succeeding charts the curves on the left were plotted by the frequent method of measurement and on the right by the infrequent method.

We have selected Charts I and II from a number of others as exemplifying the usual reactions following increasing amounts of work in a normal man. The blood-pressure curves are plotted both by the method of frequent reading and by our own method of reading at stated intervals.

The systolic blood-pressure shortly (ten to fifteen seconds) after small or moderate amounts of work is raised; it then mounts rapidly, attaining its summit generally inside of forty seconds and rapidly

[2] In our earlier work the first measurements of the blood-pressure were made between twenty and thirty seconds after work, the second measurement between fifty and sixty seconds after and the third measurements ninety seconds after. The method described in this article undoubtedly gives a more accurate representation of the blood-pressure curve.

subsides. The height of the first readings and of the subsequent rise is dependent, as a rule, on the amount of work and the time in which it is performed.

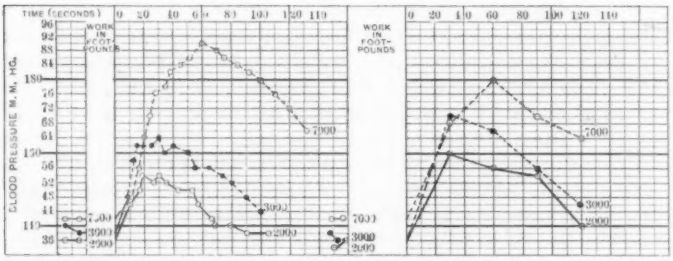

CHART II.—Blood-pressure reactions in a normal man after increasing amounts of work furnished by swinging dumb-bells. Five to ten minutes intervened between the individual exercises.

Following the greatest amounts of work the rise is delayed so that the summit is reached after fifty or more seconds and the subsidence to normal is gradual instead of rapid. This last extreme reaction is what we have termed in our earlier articles a "delayed rise." Cotton, Rapport and Lewis[3] prefer to call this a "delayed summit." The results stated above agree quite closely with their conclusions.

The time at which the pressure reaches its maximum is of considerable importance because it indicates either a rapid or slow development of the blood-pressure curve. In a normal person in good physical training the summit is reached, after all but the heaviest amounts of work, before fifty seconds have elapsed. When the work reaches the limit of effort, judging from the performer's sensations and degree of breathlessness, there ensues a delayed rise, the summit of the pressure falling somewhere between fifty and ninety seconds, and the curve then slowly subsides to normal.

The term "delayed rise" will be used, therefore, to indicate that form of the systolic blood-pressure curve which shows a delayed rise, with a summit occurring between fifty and ninety seconds after work. It presents no qualitative difference from the curves following moderate amounts of work, but is simply an exaggeration of what might be called the "normal type." An examination of the curves obtained by the infrequent method of measurement (see Chart I) shows that a delayed rise, with all that it implies as to the form of the pressure curve, will be revealed by this much simpler method with almost as much certainty as by Rapport's method.

This circulatory reaction possesses, we believe, peculiar significance, and we will enumerate the facts we have discovered about the delayed rise following work in normal people.

[3] Heart, 1917, vi, 269.

The Delayed Rise in Normal People. (*a*) In a normal person in good physical training a delayed rise is found only after heavy work, and is accompanied by marked breathlessness. The limit of effort is apparently approached when this reaction ensues.

The amounts of work which delay the summit to between fifty and ninety seconds vary for different persons according to their condition of physical training.

We have never failed to elicit a delayed rise in normal people at some stage as they performed progressively increasing quantities of work.

(*b*) A normal person in poor physical training will show a delayed rise after moderate amounts of work which are not accompanied by as marked breathlessness as is noted under (*a*).

(*c*) The production of a delayed rise is dependent on the amount of work and the time in which it is performed (power expended) and not on the group of muscles employed.[4]

(*d*) The amount of work which is followed by a delayed rise varies but little from day to day. Chart III exemplifies this.

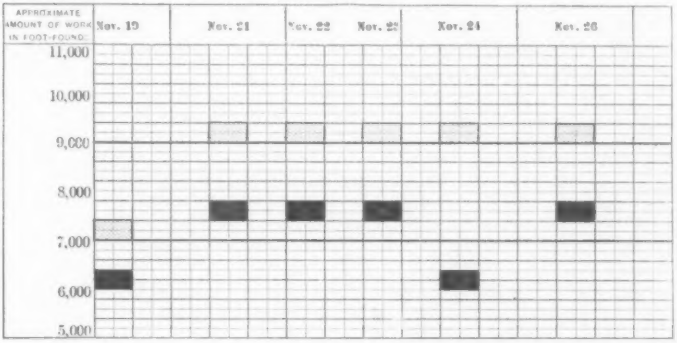

CHART III.—Daily variations in amounts of work performed by normal persons which were followed by delayed rises. The black squares represent work which was not followed by a delayed rise. Shaded squares represent work which was followed by a delayed rise.

(*e*) Children are able to perform relatively larger amounts of work without producing a delayed rise than are adults, taking into consideration their respective weights.[5] After thirty years of age the amounts of work which can be performed without evoking delayed rises gradually decrease.

(*f*) Physical training increases rapidly the amounts of work which can be performed without delayed rises ensuing.

[4] Arch. Int. Med., 1916, xvii, 366. Although not so stated, all first measurements in this article were made between twenty and thirty seconds after work.

[5] Personal communication, Dr. W. P. St. Lawrence.

(*g*) During convalescence from infectious diseases the amounts of work which can be performed without delayed rises are small at first and then increase rapidly.[6]

The Systolic Blood-pressure after Work in Patients Suffering from Marked Cardiac Insufficiency. Two patients with rhythmical pulses were selected whose cardiac reserve powers were obviously exhausted and their curves after work were plotted by both the frequent and the infrequent methods of reading the blood-pressure.

The first patient, M. W., aged twenty-one years, was suffering from an old rheumatic endocarditis which had left him with a double mitral and an aortic lesion. As he lay in bed he was dyspneic, his legs were swollen, the liver was enlarged and there were many moist rales at the base of the lungs.

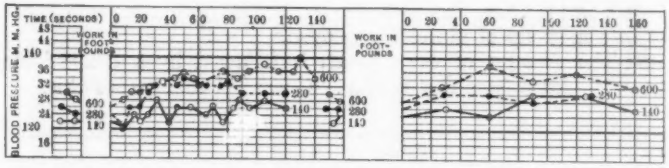

CHART IV.—Blood-pressure reactions after increasing amounts of work furnished by flexing dumb-bells in patient M. W., suffering from extreme cardiac insufficiency (reserve power = O).

The second patient, L. G., aged seventeen years, was suffering from cardiac insufficiency following a rheumatic lesion of the mitral and aortic valves. He was dyspneic as he sat in a chair, both lungs showed moist rales at the bases and his liver was enlarged. He had no pretibial edema. Chart V shows his blood-pressure reactions.

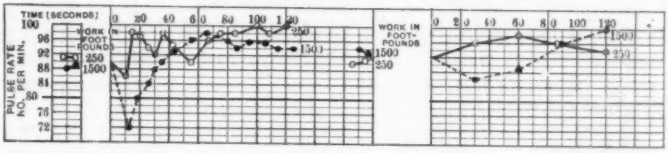

CHART V.—Blood-pressure reactions after increasing amounts of work furnished by dumb-bell movements in patient L. G., suffering from marked cardiac insufficiency (reserve power = O).

The blood-pressure curves in these charts are quite typical of the curves we have obtained in all patients suffering from grave cardiac insufficiency. The first reading is often below that noted before work. As the work is increased the first reading frequently falls lower and lower. This peculiarity is also often observed when we use the infrequent method of plotting the curve. The development of the curve is greatly prolonged, as is evidenced by the marked delay

[6] Personal communication, Dr. Hubert Mann.

in the rise. The amounts of work which produce this curve are very small as compared with those in normal subjects. Chart V shows very well the effect of a marked increase in work. Instead of mounting higher, as it would in a normal person, the initial drop of the blood-pressure was simply accentuated. The curve otherwise greatly resembles that following the much smaller amount of work.

The similarity between these curves, obtained in patients with no cardiac reserve power, and the curves with a delayed rise in normal people, is marked and affords a valuable clue to the significance of this type of blood-pressure curve.

The Systolic Blood-pressure after Work in Patients Suffering from Moderate Cardiac Insufficiency. The patient whose curves are represented in Chart VI was selected as a typical example of this class of patients. She was an ambulatory patient with mitral stenosis arising from rheumatic endocarditis. She was able to walk on the level slowly without discomfort. Going up one flight of stairs (twenty steps) caused marked breathlessness and palpitation, obliging her to stop and rest after ten steps. She had no edema of the legs or lungs.

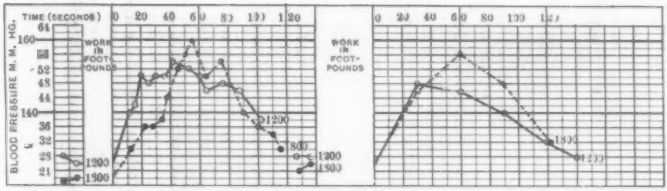

CHART VI.—Blood-pressure reactions in a patient with moderate cardiac insufficiency after increasing amounts of work furnished by dumb-bell movements. Five to ten minutes intervened between the individual exercises.

It will be noted that 1800 foot-pounds of work was followed by a delayed rise and was accompanied by marked dyspnea and palpitation. She was able to perform 1200 foot-pounds without causing a delayed rise and with but moderate breathlessness.

Improvement in Cardiac Insufficiency and its Effect upon the Delayed Rise. Patients suffering from varying degrees of cardiac insufficiency show, as they improve, a steady increase in the amounts of work they are able to perform without causing this reaction. Chart VII exemplifies the foregoing statement.

The Significance of the Delayed Rise in Systolic Blood-pressure. The primary meaning of this reaction is that the curve of the systolic blood-pressure, if plotted out, would have the form described and depicted in the first part of this article.

In order to appreciate the significance of this form of the blood-pressure curve the facts we have enumerated about this reaction in normal people must be considered. Of these the most important

are the invariability of the delayed rise after a stated amount of work performed in a stated time quite irrespective of the group of muscles

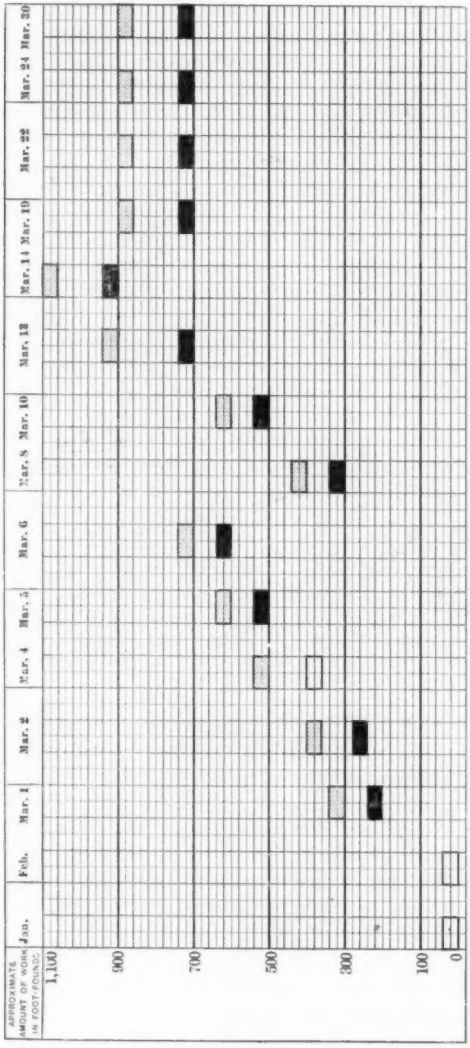

CHART VII.—The increase in the amounts of work performed by the patient G. C. which were not followed by delayed rises. This patient at the outset suffered for one month from extreme cardiac insufficiency, and, coincident with the work increase, his clinical condition improved markedly. The black squares represent work which was not followed by a delayed rise; the shaded squares, work which was. The empty squares indicate that any work whatsoever was followed by a blood-pressure curve similar to those in Charts IV and V.

employed; the small variations from day to day of the quantities of work which cause this reaction; the relatively greater amounts of

work which children, as compared to adults, can perform, taking their respective weights into consideration, before this reaction ensues; and the marked effect which physical training has in increasing the amounts of work a person can accomplish without evoking a delayed rise.

It is the type of curve obtained after minimal amounts of work in patients with no cardiac reserve power, however, which does most to make clear the meaning of this reaction in healthy people. These curves always show a delayed rise with a very slow return to normal, and are quite similar to the curves initiated by a delayed rise in normal persons.

TABLE I.—PULSE REACTIONS IN NORMAL MEN.

Patient.	Work.	Pulse rate.		Return to normal, seconds.	Delayed rise, systolic pressure.	Delay, seconds.
		Before.	Immediately after.			
J. M., aged twenty-four years.	20 S. 5	96	112	120	No	
	20 S. 10	72	118	180	No	
	30 S. 10	80	120	180	Yes	58
	20 S. 20	88	128	240	Yes	60
	20 S. 30	88	140	300	Yes	60
A. Q., aged twenty-six years.	15 S. 10	72	104	120	No	
	15 S. 15	72	108	118	Yes	60
	15 S. 20	70	104	120	No	
	20 S. 20	88	128	120	Yes	60
	30 S. 20	68	124	300	Yes	60
	30 S. 20	68	112	120	No	
	30 S. 25	72	128	120	No	
	30 S. 30	84	112	180	Yes	60
	30 S. 20	84	112	180	No	
	30 S. 25	88	136	120	Yes	60
	30 S. 35	88	136	240	Yes	60
R. O., aged twenty-three years.	20 S. 10	104	128	120	No	
	20 S. 15	104	140	180	No	
	20 S. 25	104	158	180	Yes	60
	20 S. 35	104	156	240	Yes	60
W. M., aged twenty-two years.	20 S. 15	90	112	180	No	
	20 S. 20	96	128	120	Yes	60
	20 S. 25	96	124	120	Yes	60
R. T., aged forty-one years.	20 S. 30	88	120	150	No	
	20 S. 35	84	136	240	No	
	20 S. 40	84	140	300	No	
	20 S. 45	84	148	360	Yes	60

The effect of work upon the pulse rate of normal men. There was a period of from five to ten minutes between the individual exercises. The figures 120 in the column headed "Return to Normal" means that the rate became normal after two minutes *or earlier*.

Another fact which has an important bearing on this question is that, coincident with the improvement of patients suffering from cardiac insufficiency, there occurs an increase in the amounts of work they can perform without producing delayed rises.

There is but one conclusion, it seems to us, which can be drawn

from these facts, and that is that a delayed rise of systolic blood-pressure, with all that it implies as to the form of the pressure curve, means that the preceding work has either overtaxed or is on the point of overtaxing the heart's reserve power. If this conclusion is correct it is a simple matter to use comparisons of the amounts of work causing the delayed rise as an indirect measure of the cardiac reserve power.

TABLE II.—PULSE REACTIONS IN PATIENTS WITH CARDIAC INSUFFICIENCY.

Patient.	Work in foot pounds.	Pulse rate.		Return to normal, seconds.	Delayed rise, systolic pressure.	Delay, seconds.
		Before.	Immediately after.			
J.S., aged twenty-seven years. Marked cardiac insufficiency. Reserve power zero.	200	100	116	180	Yes	90
	200	116	124	120	Yes	120
	300	112	120	120	Yes	120
	300	120	128	120	Yes	88
M. W., aged twenty-seven years. Marked cardiac insufficiency. Reserve power zero.	60	104	108	120	Yes	60
	140	108	116	180	Yes	90
	280	112	112	120	No	
	400	112	116	120	Yes	120
	400	106	112	120	Yes	88
	450	112	120	180	Yes	120
	140	108	116	125	Yes	90
	280	106	118	120	Yes	85
	600	112	118	120	Yes	60
	140	108	110	120	No	
	200	108	114	120	Yes	58
	200	108	118	120	Yes	90
L. G., aged seventeen years. Moderate insufficiency.	600	84	104	120	Yes	90
	1200	88	112	120	Yes	90
	250	66	80	120	No	
	375	64	76	120	Yes	90
	500	64	80	120	Yes	90
	750	68	88	120	Yes	58
	1200	76	108	120	Yes	88
	250	84	88	120	Yes	60
	500	72	80	120	Yes	60
	750	76	104	180	Yes	60
	200	72	100	120	No	
	500	76	100	180	No	
	750	80	100	120	Yes	90
	1200	78	118	118	Yes	88
	2000	78	132	240	Yes	90
	250	90	102	120	Yes	60
	900	90	112	300	Yes	118
	1400	92	128	180	Yes	120
S. T., aged fifty-eight years. Moderate cardiac insufficiency.	700	76	88	120	No	
	2000	74	96	120	Yes	90
E. C., aged thirty-four years. Moderate cardiac insufficiency.	170	92	108	120	No	
	340	88	80	...	No	
	1100	84	104	120	No	
	2000	80	...	180	Yes	60

The effect of work upon the pulse rate of patients suffering from varying degrees of cardiac insufficiency. Five to ten minutes intervened between the individual exercises. The figure 120 in the column headed "Return to Normal" means that the rate became normal after two minutes *or earlier*.

The Effect of Work upon the Pulse Rate in Normal Indiriduals. It has been our experience that changes in pulse rate following work have seldom afforded any reliable indication as to the condition of the heart's reserve power. Recently, Mekins and Gunson[7] have published their investigations upon the effect of exercise on the pulse rate in patients suffering from "disordered action of the heart." One of their conclusions was that patients in whom the pulse rate did not return to normal within a short period of time (*i. e.*, two minutes) performed the simplest exercises with difficulty. With this particular conclusion in mind we have observed the pulse rate after work in a few normal people and in a few patients with cardiac insufficiency.

The pulse was counted before exercise and then for fifteen seconds immediately after exercise. At the end of one hundred and ten seconds it was then counted again for twenty seconds. From these counts the rates per minute immediately after work and at the end of one hundred and twenty seconds were calculated. If the rate at the end of two minutes was within six beats of the pre-exercise rate it was considered to have returned to normal. Table I summarizes our results in normal people.

There were 27 experiments carried out on five normal men. A delayed rise of the systolic pressure occurred fourteen times and was accompanied nine times by a pulse rate which did not return to normal inside of two minutes. Thirteen times there was no delayed rise, and yet on seven occasions the pulse rate did not return to normal inside of two minutes.

The Effect of Work upon the Pulse Rates of Patients Suffering from Varying Degrees of Cardiac Insufficiency. Table II summarizes our results in patients who had either a moderate or no cardiac reserve power.

There were 40 experiments carried out on 5 patients. A delayed rise of the systolic pressure occurred 31 times and was accompanied 9 times by a pulse rate which did not return to normal inside of two minutes. Twenty-two times the pulse rate returned to normal two minutes or sooner after work.

The results of these experiments, carried out on normal persons and those suffering from cardiac insufficiency, few in number though they are, tend to confirm our belief that the time required for the pulse rate to return to normal affords but little information, in either normal people or patients with cardiac insufficiency, as to the condition of the heart's reserve power.

CONCLUSIONS. The occurrence of a delayed rise in systolic blood-pressure after work indicates that the preceding work has either overtaxed or is on the point of overtaking the heart's reserve power. The presence of a delayed rise can be determined by the

[7] Heart, 1917, vi, 285.

infrequent method of plotting the pressure curve with almost as much certainty as by the frequent method.

A small number of experiments upon normal people and upon patients with cardiac insufficiency showed that no definite relation existed between the time required for the pulse rate to return to normal and the condition of the cardiac reserve power.

We wish to express our thanks to Dr. William R. Williams, whose hospital service furnished the material for the foregoing work, for his advice and coöperation in carrying out the same.

PERFORATED GASTRIC AND DUODENAL ULCER: A STATISTICAL REPORT OF FIFTY-NINE CASES.

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(From the Clinics of the Cook County Hospital.)

During the last six years (1911 to 1916 inclusive) there were 59 cases of perforated gastric and duodenal ulcer admitted to the Cook County Hospital. Of these cases 48 were perforated gastric ulcers and 11 perforated duodenal ulcers. During this same period the total number of ulcer cases was 506 gastric ulcers and 72 duodenal ulcers. The frequency of perforation in these cases was 9.4 per cent. in gastric ulcer and 15 per cent. in duodenal ulcer. The patients were seen at varying periods of time after the perforation, some shortly after while others were moribund and in shock. Only those cases in which the perforated ulcer was seen at operation or at autopsy are included in this series. All cases of doubtful diagnosis have been excluded in order to make the data more accurate. Forty-nine of the patients were operated upon by ten different staff surgeons. In the remaining 10 cases the ulcer was recognized at autopsy.

Age and Sex Incidence. Of the perforated gastric ulcers 44 were in males and 4 in females. Caird[1] in a series of 247 cases from the Edinburgh Hospital found a greater percentage of perforated gastric ulcers in females. Connors[2] in a series of 41 cases found 36 in males and 5 in females. The perforated duodenal ulcers were all in males. This agrees with the findings of Caird,[3] who reported 179 males and 21 females in a series of 200 cases.

The majority of the perforations occurred between the ages of thirty and forty years in gastric ulcer and between twenty and thirty years in duodenal ulcer, as will be noted in the following table:

Age.	Gastric ulcer.	Duodenal ulcer.
Under 20 years	1 cases	0 cases
20 to 30 "	12 "	7 "
30 to 40 "	19 "	2 "
40 to 50 "	9 "	2 "
50 to 60 "	4 "	0 "
60 to 70 "	3 "	0 "

The occupation of the patient did not seem to have any bearing, as many trades were represented, and none that would seem at all a predisposing factor.

Previous Gastric Disturbance. It is difficult to obtain an accurate history of any previous stomach trouble when the patients are first seen, due to their acute suffering. The majority, however, recall some previous gastric disturbance. In this series, 29 cases of gastric and 6 cases of duodenal ulcer gave a history of previous trouble of variable duration.

Duration.	Gastric ulcer.	Duodenal ulcer.
Under 1 year	5 cases	2 cases
1 to 5 "	11 "	4 "
5 to 20 "	3 "	0 "
No duration noted	10 "	0 "

Sixteen cases of perforated gastric and 5 cases of duodenal ulcer gave no history of previous gastric disturbance. This may not be a true statement, as the patient's condition was often extremely grave, and the history consequently was rather hurriedly and briefly obtained. Often the patient agreed to any question asked, so that many contradictory facts were obtained. Oftentimes slight stomach complaints, as heartburn or slight discomfort after meals, were never thought of by the patient when asked if he had any previous stomach trouble, and were elicited only on careful inquiry. However, it is true that there may be an entire absence of any antecedent indigestion and the perforation may occur without warning.

Premonitory Symptoms. There are no characteristic prodromal symptoms which may give warning that perforation is about to occur. In several cases it was noted that the symptoms of indigestion were worse than usual for several days preceding the perforation, but such exacerbations are not infrequently experienced in gastric disorders apart from perforation. Many cases gave no prodromal symptoms whatever. In this series 27 cases of gastric and 2 cases of duodenal ulcer gave variable prodromal symptoms. The most constant symptom was pain, usually slight, located in the upper abdomen, and in some cases associated with food taking. Vomiting occurred in several cases. Two cases gave a history of alcoholic excesses previous to the perforation.

Determining Cause. No single factor can be assigned as being the determining cause of the rupture. In 7 cases the perforation occurred while doing heavy work. It is conceivable that severe muscular effort might have determined the actual rupture of an ulcer, the base of which was already weakened. In several cases perforation occurred shortly after eating, but in a considerable proportion of the cases it occurred from six to ten hours after food was taken, so that the entrance of food into the stomach did not always appear to have a determining influence.

Onset. In practically every case the onset was sudden, with agonizing pain in the epigastrium, often doubling up the patient on account of the extreme severity. Brunner[4] in a series of 263 cases of gastric and 52 cases of duodenal ulcer reported there was an acute onset of pain in 260 of the gastric ulcer cases and in 49 of the duodenal ulcer cases. In a great majority of the cases the pain was located in the epigastrium. In gastric ulcer the point of maximum intensity was generally a little to the left of the midline, while in duodenal ulcer it was a little to the right. In a few cases the pain was generalized or was localized in the lower abdomen.

Location of pain.	Gastric ulcer.	Duodenal ulcer.
Epigastrium	37 cases	9 cases
Generalized	3 "	2 "
Lower right side	3 "	0 "
Lower left side	1 "	0 "

Vomiting occurred in 35 cases of perforated gastric ulcer shortly after perforation and in 6 cases of duodenal ulcer. Several patients were nauseated, but did not vomit.

Period of Reaction. Following the sudden onset of pain there is a period of remission coming on from two or three hours after the perforation. This was noted in a large proportion of the cases. The acute symptoms abate and the patient looks and feels better. The physician called in at this time may not recognize the seriousness of the condition and delays sending the patient to a hospital. The recurrence of pain indicates the onset of peritonitis. Kennedy[5] recognizes three periods following perforation: (1) the stage of shock and collapse; (2) the stage of reaction; (3) the stage of diffuse peritonitis. It is during the second stage or the period of remission that the diagnosis is most difficult, but a mistake may not be serious if the patient is operated upon at once and the true condition recognized.

Findings. Many patients were not seen until some time after perforation had occurred. Eight cases of gastric and 2 cases of duodenal ulcer were moribund on entrance. In the majority of cases seen early the point of maximum tenderness corresponded closely to the point of maximum pain. In late cases the tenderness was generalized.

Location of tenderness.	Gastric ulcer.	Duodenal ulcer.
Epigastrium	24 cases	5 cases
Generalized	23 "	5 "
Right lower	1 "	1 "

Rigidity was present in practically every case, though of varying degree, and was especially marked in the upper abdomen. Tympanites was noted in 16 cases of gastric and in 6 cases of duodenal ulcer. Fluid was diagnosed in 14 cases of gastric and in 6 cases of

duodenal ulcer. Schoemaker[6] has pointed out that in percussing fluid in the flank an increase of pressure on the percussed finger displaces the fluid, bringing the intestines closer, and thus a tympanitic note is elicited. As a result small amounts of fluid may be overlooked. Thirteen cases of gastric ulcer were in shock on entrance, with rapid pulse, pallor and a subnormal temperature. Few cases showed a febrile reaction; these were late cases with a generalized peritonitis. The pulse and leukocytes are given in the following table:

Duration of perforation.	Cases recovering. Pulse.	Cases recovering. Leukocytes.	Cases fatal. Pulse.	Cases fatal. Leukocytes.
Under 5 hours	86	13,600		
5 to 15 "	108	13,300	128	10,100
15 to 24 "	80	15,600	106	20,000
Over 24 "	98	17,900	112	18,600

In early stages the pulse was not much increased in rate, though there was a moderate increase in the leukocyte count. In later stages the pulse became more rapid and the leukocytes increased slightly. It is worthy of note that in the cases recovering the pulse was never as rapid as in the cases which resulted fatally. This was probably due to a more virulent peritonitis and a greater degree of shock in those cases. Petrén[7] noted that the pulse was slower in the early stages and that the percentage of mortality was less in cases with a slow pulse. This will be noted in the following table from his report:

	Pulse frequency.
1 to 5 hours	80 to 100 per minute
5 to 10 "	90 to 110 "
10 to 15 "	110 to 120 "

	Pulse rate.	Recovery.	Death.
21 cases	80 to 100	16 cases	5 cases
7 "	104 to 120	5 "	2 "
2 "	125 to 140	0 "	2 "

Certain early cases had a high leukocyte count with a pulse below 90. Finney[8] considered a leukocytosis in a young person with a history of previous gastric disturbance as a diagnostic sign of considerable importance.

Diagnosis. The diagnosis made before operation in this series of cases is noted in the following table:

Diagnosis.	Gastric ulcer 48 cases.	Duodenal ulcer 11 cases.
Perforated gastric ulcer	21 times	3 times
Perforated duodenal ulcer	2 "	1 "
Acute appendicitis	6 "	3 "
Acute cholecystitis	3 "	0 "
Acute abdomen (peritonitis)	13 "	4 "
Ileus	2 "	0 "
Liver abscess	1 "	0 "

The diagnosis was not difficult when the case was seen early and a good history obtained. The conditions with which perforation was

most frequently confused were, in the early stages, acute appendicitis, acute cholecystitis and acute pancreatitis, and in the late stages ruptured appendix and general peritonitis from an unrecognized source. The absence of a febrile reaction in the early stages and the history of a sudden, agonizing pain helped to differentiate from other acute abdominal conditions.

In appendicitis the onset of the pain is more gradual, its location is in the lower right side and it is preceded by a rise in temperature. Acute cholecystitis is more difficult to distinguish, though the pain is located somewhat farther out from the midline. Acute pancreatitis is relatively infrequent and is therefore rarely confused.

In several of the cases an incision was made for an appendectomy, and only upon opening the abdomen was the perforation recognized. In a perforated ulcer the fluid is uniform and is usually more abundant as the upper abdomen is exposed, while in appendicitis the fluid becomes thicker and more purulent as the appendix is approached. The appendix itself presents greater gross changes.

In the late cases, when the tenderness and rigidity were generalized, a correct diagnosis was made, as a rule, only upon exploratory incision. A history of previous gastric disturbance and the location of the pain in the epigastrium at the onset helped to place the source of the peritonitis in the upper abdomen. Methylene blue[9] was given by mouth in several cases of suspected perforation before operation, and the finding of stained free fluid upon opening the abdomen confirmed the diagnosis.

Operation. An operation was performed in 40 cases of gastric and in 9 cases of duodenal ulcer. Many were in late stages and in shock when operated, and survived for only a short time. The remaining 10 patients were in such serious condition when seen that no operative procedure was thought advisable.

Fluid. As a rule the peritoneal cavity contained a variable amount of fluid. It was present in 37 cases of gastric and in 9 cases of duodenal ulcer. The character varied with the duration of the perforation. In early cases it was serous and at times bile-stained. In late cases it was thicker and seropurulent. Free stomach contents were noted in 10 cases of gastric and in 3 cases of duodenal ulcer. In 2 cases of perforation through the posterior wall of the stomach the fluid was limited to the lesser peritoneal cavity. In 1 case the fluid was purulent and limited by dense adhesions about the duodenum.

Associated with the fluid was a peritonitis of varying grades, depending upon the duration of the perforation. In early cases the surface was reddened and inflamed, while in late cases it was covered with a fibrinous exudate.

Site of Perforation. The most common site of perforation in gastric ulcers is on the anterior wall of the stomach near the pylorus along the lesser curvature. The perforation was anterior, near the pylorus in 43 cases, anterior in cardia in 1 case, and posterior in 4

cases. Multiple perforating ulcers were noted in 2 cases. The perforating ulcer of the cardia was associated with a carcinoma of the stomach wall. Caird[1] in 228 cases found the perforation on the anterior wall in 209 cases and on the posterior wall in 19 cases. In all cases recovering after operation the ulcer was located anterior near the pylorus. All cases on the posterior wall resulted fatally. Induration was present about the ulcer in practically every case.

In all the cases of duodenal ulcer the perforation was anterior in the first portion near the pylorus. Multiple ulcers were present in one case, but only one was perforated. Caird[3] in 118 cases noted the perforation on the anterior surface in 101 cases, on the superior surface in 13 cases and on the posterior surface in 4 cases. The size of the perforation in both gastric and duodenal ulcer was variable. The larger ones were generally more fatal.

Procedure. In the majority of cases a simple closure of the perforation by Lembert suture and drainage was done. Other procedures were employed in a few cases.

Procedure.	Cases.	Recovery.	Death.
Gastric ulcer.			
Closure and drainage	26	12	14
Closure and gastro-enterostomy	5	4	1
Excision and suture	1	0	1
Drainage, not closed	5	0	5
Closure, no drainage	1	0	1
Gastrostomy	1	0	1
No operative record	1	0	1
Duodenal ulcer.			
Closure and drainage	5	4	1
Closure and gastro-enterostomy	3	1	2
Drainage, not closed	1	0	1

In 5 cases of gastric and in 1 case of duodenal ulcer simple drainage was done, as the patient's condition was so grave that no further procedure was deemed advisable; all resulted fatally. In 1 case a rubber tube was inserted into the stomach through the perforation, and in 5 cases of gastric and in 3 cases of duodenal ulcer a primary gastro-enterostomy was done in addition to closure of the perforation, with 5 recoveries. The advisability of doing a routine gastro-enterostomy at the time of repair of the perforation has been widely discussed. Eliot[10] has given an excellent review of this subject, and is of the opinion that a gastro-enterostomy is indicated only when the lesion itself is of such an extent that its suture or subsequent cicatricial deformity would lead to a persistence or recurrence of symptoms.

Immediate Results. Of the 40 cases of perforated gastric ulcer operated upon 16 recovered and 24 died, and of the 9 cases of duodenal ulcer 5 recovered and 4 died. Many patients died in shock within the first twenty-four hours following the operation. Others continued weak for days afterward and finally succumbed to general peritonitis. The cause of death and complications in the operated cases are given in the following table:

Cause of Death. Gastric Ulcer (24 cases).

Eighteen cases with closure of perforation.

2 cases died under anesthetic.
7 cases died in shock within twenty-four hours.
6 cases died of generalized peritonitis.
1 case died of subphrenic abscess.
1 case died after partial closure of ulcer.
1 case died after perforation of second ulcer.

Six cases with no closure.

1 case died in shock in twenty-four hours.
1 case had carcinoma of cardia also.
1 case developed peritonitis after gastrostomy.
3 cases developed general peritonitis, all posterior ulcers.

Duodenal Ulcer (4 cases).

2 cases died in shock in eighteen hours.
2 cases died of general peritonitis.

Hours Elapsing after Perforation until Operation. The patients were operated upon at different periods of time after perforation, and it will be seen from the following table that those operated within the first twelve hours had a greater percentage of recoveries:

Gastric ulcer.	Cases.	Recovery.	Death.
Under 5 hours	4	4	0
5 to 15 "	13	7	6
15 to 24 "	9	2	7
Over 24 "	14	3	11
Duodenal ulcer.			
Under 5 hours	1	1	0
5 to 12 "	2	1	1
12 to 24 "	3	2	1
Over 24 "	3	1	2

Mortality. The mortality of the operated cases was 60 per cent. in gastric ulcer cases and 44.4 per cent. in duodenal ulcer cases. The mortality, including cases not operated upon, was 66.6 per cent. in gastric ulcer cases and 55.5 per cent. in duodenal ulcer cases. Caird[13] gave the mortality as 42.5 per cent. in 247 cases of gastric ulcer and as 39.5 per cent. in 200 cases of duodenal ulcer. Collinson[11] gave the mortality as 53.8 per cent. in 13 cases of gastric ulcer and as 32.5 per cent. in 40 cases of duodenal ulcer. The mortality is directly proportionate to the length of time elapsing after the perforation.

Mortality.	Gastric.	Duodenal.
Cases operated upon under 5 hours	0.0 per cent.	0.0 per cent.
" " " 5 to 15 "	46.1 "	50.0 "
" " " 15 to 24 "	77.0 "	33.3 "
" " " over 24 "	78.5 "	66.6 "

The fact that cases operated upon after twenty-four hours do recover is due to the localizing of the infection. Walker[12] in 78 cases gave the mortality of cases operated upon in from five to twelve hours as 17.9 per cent.; twelve to twenty-four hours as 46.6 per cent., and over twenty-four hours as 66.2 per cent. Connors[2] in

42 cases gave the mortality as 20 per cent. in cases operated upon under six hours and as 66 per cent. in cases over six hours.

In 16 cases of gastric ulcer which recovered after operation, 11, or 68.7 per cent., were operated upon within fifteen hours after perforation had occurred. In the 24 cases which resulted fatally only 6, or 25 per cent., were operated upon within fifteen hours. This is similar to the findings of Caird[1] in his series of cases. In cases which recovered 65.9 per cent. were operated upon within twelve hours, while in cases which were fatal only 34.6 per cent. were operated upon in that time.

In 5 cases of duodenal ulcer which recovered, 3, or 60 per cent., were operated upon in the first twelve hours, while in the 4 cases resulting fatally only 1, or 25 per cent., was operated upon in the first twelve hours. Caird[2] in a series of 200 cases found that in the cases which recovered 73.1 per cent. were operated upon in the first twelve hours, while in the cases which resulted fatally only 37.6 per cent. were operated upon in that time.

COMMENT. From a study of these cases it becomes evident that an early recognition of the condition followed by an immediate operation is necessary for the best results. This is well illustrated by the fact that all cases diagnosed and operated upon within the first five hours recovered, while in those operated later there was a mortality proportionate to the delay. The diagnosis should be made when the patient is first seen if possible and immediate operation insisted upon. The difficulty in diagnosis is due to the period of reaction that follows the acute onset, during which time the patient appears so much better that the seriousness of the condition is overlooked. This point cannot be too strongly emphasized, as a large proportion of the delayed cases entering the hospital are due to the mistaken opinion of the attending physician. The diagnosis is too often that of a mild colic which is expected to pass away in time, but instead symptoms of peritonitis develop, and only then is the seriousness of the condition recognized. Even in delayed cases an operation should be performed, for otherwise the result is almost invariably fatal.

Considerable confusion in the diagnosis of perforation arises from the fact that the patient presents a markedly different clinical picture in the various stages. The symptoms are not progressive and the physical signs are not well developed until comparatively late.

At the onset, during the stage of shock, the patient is pale and faint, with an anxious expression on the face, and holds the body absolutely rigid on account of the intense abdominal pain. The marked severity of the pain is thought by some to be due to the chemical irritation of the peritoneum by the escaping stomach contents. The abdominal wall is retracted and so extremely rigid that very little can be determined on examination. The breathing is short and quick, and is of the costal type. Vomiting may be present, but is not of much significance, as it may be absent in per-

foration and present in so many other conditions. The leukocyte count is normal or may be slightly increased; the temperature is usually normal or may be subnormal. Perforation should not be ruled out because of a slow pulse and a normal temperature, or because of a normal or an increased leukocyte count, as these are frequent findings in this stage.

Following the acute onset there may be a period of remission during which the patient feels much better. The patient relaxes and breathing is much easier. The abdomen is less rigid, though there is a local rigidity in the upper abdomen and a tenderness confined to the region of the perforation. On careful examination fluid may be demonstrated in the flank, which is a very valuable sign. The pulse is still slow but gradually increases in frequency. The temperature also rises slightly. Diagnosis in this stage depends largely on the history of the onset. An acute attack of violent abdominal pain associated with shock and followed by a period of improvement is always significant.

Finally the symptoms of peritonitis become evident. The patient is restless, with sunken eyes and a drawn, facial expression. The abdomen becomes distended and the liver dulness is diminished. Fluid is not so easily demonstrated. The pain and tenderness are generalized and the rigidity is now board-like. The pulse is rapid and wiry, the leukocytes greatly increased and a febrile temperature present. The diagnosis of peritonitis is easily made, but the source presents greater difficulty. The tenderness may be most marked in the right iliac fossa, due to the gravitation of the fluid, and a diagnosis of appendicitis is made. A careful history and examination aid in differentiating, but usually an exploratory incision is necessary to determine the condition. Cases simulating perforation should have careful consideration before this possibility is excluded.

BIBLIOGRAPHY.

1. Perforated Gastric Ulcer, Edinburgh Med. Jour., 1914, xiii, 455.
2. Observations of forty-two Cases of Perforated Gastric Ulcer, Am. Jour. Surg., 1916, xxx, 173.
3. Perforated Duodenal Ulcer, Edinburgh Med. Jour., 1913, xi, 405.
4. Die acut in die freie Bauchhöhle perforirende, Magen- und Duodenalgeschür., Deutsch. Ztschr. f. Chir., 1903, lxix, 101.
5. Latent Period in Acute Perforations of Stomach or Duodenum, Lancet, 1917, i, 410.
6. Schoemaker, J.: Ueber Magenperforation, Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1909, xx, 21.
7. Petrén, G.: Ueber Perforation von Magen- und Duodenalgeschwüren, Beitrage f. klin. Chir., 1911, lxxii, 319.
8. Finney, J.: Perforating Ulcer of Stomach, Ann. Surg., 1900, xxxii, 1.
9. Baker, H.: Methylene Blue in Diagnosis of Acute Perforating Gastric and Duodenal Ulcers, Surg., Gynec. and Obst., 1917, xxv, 695.
10. Eliot, E.: Clinical Features and Treatment of Acute Perforating Gastric and Duodenal Ulcer (a full bibliography follows this article), Ann. Surg., 1912, lv, 546.
11. Collinson, H.: Some Present-day Problems in Surgery of Gastric and Duodenal Ulcer, Jour. Am. Med. Assn., 1914, lxiii, 1184.
12. Acute Perforation of Ulcer of Stomach and Duodenum, Med. Press and Circ., 1915, c, 605.

WAR MEDICINE

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THE TACHYCARDIAS OF SOLDIERS.

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IN the present war it has been the experience of the European combatants that many men have broken down during the stress of active campaigning as a result of damaged or insufficient hearts which were unable to bear the additional strain thrown upon them by the campaign. Many of these heart cases were invalided home on account of frank cardiac disease, valvular disease unrecognized through insufficient examination at the time of the physical examination upon entering the army or myocardial disorders unsuspected or developing after entry into the army. There were, however, many returned to home hospitals

in whom actual organic cardiac disease could not be demonstrated, yet who suffered from a group of symptoms which were for the most part almost entirely referable to the cardiovascular apparatus and to which various terms have been applied, suggestive of the part played by the heart in producing and maintaining these symptoms. This symptom-complex is referred to by the English as "disordered action of the heart (D. A. H.)," as the "irritable heart of the soldier," as "soldier's heart" and as "effort syndrome." The terms are very inclusive, and practically any case with subjective cardiac symptoms, no matter what the cause, sufficiently severe to prevent the man carrying on his duties as a soldier, is listed as D. A. H., provided that the objective symptoms are not sufficiently marked to enable the physician to label the disorder as a definite nosological entity. As a result of this rather indiscriminate filing of indefinite cases into the one cabinet there is considerable confusion in the English and French literature as to just what is "soldier's heart." Certainly there is decided confusion as to the pathogenesis of the condition and as to what cases should be included etiologically. Most observers are, however, united in describing the same group of symptoms for the condition, but are divided, necessarily, owing to the obscurity of the etiology, upon the question of proper treatment and the management of these cases.

There is one outstanding and notable symptom not only in organic cardiac disease but also in disordered heart action cases, and that is rapidity of the pulse. It is almost a *sine qua non* for the diagnosis of these latter cases. Because of this and because of the ease with which it is appreciated in physical examination it is an extremely important symptom, but unfortunately one which may be interpreted in many ways. A rapid pulse is only a symptom, and it may be indicative of an infection, of disordered nervous mechanism or of a disturbance of the endocrine system as well as pointing to the heart itself.

On account of the large number of soldiers with tachycardia that were referred for opinion during the course of the cardiovascular examinations of the 38th Division at Camp Shelby, it was thought advisable to devise a working classification for these cases in order to attempt to classify them, with the idea that these sufferers with tachycardia could be grouped into one of several etiological classes and that the subsequent course in the army of these men could be followed from the stand-point of their ability to carry on their duties as a soldier. The latter part of this paper will deal with the classification that was used during the examination. In the first portion of the article will be discussed the English and French experiences with soldiers suffering with tachycardia, and more especially "disordered action of the heart" or "soldier's heart."

Soldier's Heart.

The recognition of this syndrome by no means is original to the present war, but was first described by Dr. Henry Hartshorne,[1] to be followed several years later by the classical paper of J. C. Da Costa,[2]

[1] On Heart Disease in the Army, Tr. Coll. Phys., Philadelphia, Am. Jour. Med. Sc., 1864, xlviii, 89.

[2] On Irritable Heart. A Clinical Study of a Form of Functional Cardiac Disorder and its Consequences, Am. Jour. Med. Sc., 1871, lxi, 17.

who describes the symptom-complex most accurately; in fact, his description tallies closely with the present-day picture of the disorder. In the succeeding years there has been more or less written about "soldier's heart," and none of it of much value. Although war broke out in 1914, the first reference to the condition is in an article by Magnus-Levy,[3] who notes the frequency with which the wounded complain of dyspnea, precordial pain and palpitation, and with which they show a tachycardia, poor response to exercise, increase in the area of cardiac dulness and systolic murmurs. This article was followed by many others in the German literature. In English literature the earliest reference to the condition is in an editorial of the *British Medical Journal*, July 17, 1915. In November, Thomas Cotton, Thomas Lewis and F. H. Thiele[4] published a short note on the occurrence of bacteria in the urine of sufferers with irritable heart. Succeeding this article has come forth a veritable stream of articles on the subject, culminating in the splendid, thorough, comprehensive and scholarly study of Thomas Lewis and his co-workers working under the auspices of the Medical Research Committee.[5] In this monograph all the various phases of the subject are considered in detail and a large amout of clinical and experimental work incorporated, so that one interested in the subject will find there an extremely complete discussion of the etiology, symptomatology, pathology, prognosis and treatment of soldier's heart.

It will be advisable to digest in brief this report and to incorporate the opinion of others upon these subjects.

DEFINITION. Major Meakins,[6] Lewis and their associates give the following definition of "irritable heart of soldiers:" "We use it (the term irritable heart) to describe those patients in whom few or none of the graver signs of heart affection can be detected but in whom there is complaint of breathlessness, palpitation, giddiness or actual fainting, easy exhaustion and precordial pain in varying degree, symptoms arising for the most part under exertion or exaggerated by it."

In later publications Lewis prefers to use the term "effort syndrome," believing that it is unwise to label this group of symptoms with a term which suggests to the soldier and to others that the heart is primarily at fault.

A somewhat more comprehensive definition of soldier's heart than the one recorded above might be given. A syndrome of symptoms referable for the most part to the heart, induced by too strenuous preliminary training or the mental and physical stress of actual warfare appearing in those soldiers who have suffered a recent infection and predisposed to by various factors of varying value, such as previous sedentary life, larval hyperthyroidism, indetectable myocardial disease or congenital myocardial insufficiency, unstable nervous system, subject to neuroses of different types, and excessive smoking (?)

[3] Berl. klin. Wchnschr., January 11, 1915.

[4] A Note on the Irritable Heart of Soldiers, British Med. Jour., November 13, 1915, p. 722.

[5] Report upon Soldiers Returned as Cases of Disordered Action of the Heart (D. A. H.) or Valvular Disease of the Heart (V. D. H.), 1917. London: Causton & Sons.

[6] A Memorandum upon Heart Affections in Soldiers, British Med. Jour., September 23, 1916, p. 418.

ETIOLOGY. *Previous Occupation.* In Lewis's series of 543 cases 57 per cent. were engaged in sedentary occupations, 20 per cent. in moderately severe physical occupations and 23 per cent. in hard manual labor before entering the service. It is noteworthy that those used to hard physical work make the most satisfactory recovery.

Infection. Lewis lays particular stress upon infection as the most important etiological factor. In from 50 to 60 per cent. of his cases infection played an important role. It was during the convalescence from an acute infection that the symptoms first appeared in the greatest number of cases. Others had suffered previously from some acute infectious disease of marked severity, as pneumonia, rheumatism, typhoid fever. John Parkman[7] in a series of 40 cases found in 12 patients a previous history of an infection which may have been the exciting cause of the condition. Seven said they had had scarlet fever in childhood and 5 developed symptoms immediately following an illness in military service. Sir James Mackenzie[8] says that in the examination of about 400 cases of soldier's heart he has attributed the majority of these cases to bacterial and toxic influences. R. McN. Wilson[9] is in complete accord with Mackenzie, and L. Gallavardin[10] agrees that infections have a very decided influence upon the development and exaggeration of nervous tachycardias.

Shock. This was an immediate cause in only 2 per cent. of Lewis's cases, shock in all likelihood acting as a remote cause on a condition already existing.

Wounds and Other Accidents. These factors were present in 5 per cent. of Lewis's series. As in shock these accidents probably act much the same way. Added to this there is the added factor that most wounds are associated with infection.

Poisoning by Gas. This cause instituted the onset of symptoms in 3 per cent. of the Hampstead Hospital cases. Price and Hunt have called attention to the fact that certain gases may induce the syndrome either as a result of the action of the gas on the nervous system or else as a result of the febrile pulmonary complications of gas poisoning.

Sudden Overstrain. The occurrence of this factor was relatively rare, less than 1 per cent., in causing the onset of symptoms. A. Abrahams[11] is not in accordance with this view, he believing that this is responsible, in a fairly large number of cases, for the complex.

SYMPTOMATOLOGY. Mackenzie's[12] description of the onset of symptoms deserves to be quoted: "The account given of the onset of the symptoms is peculiarly instructive. They will say they were in the trenches and felt well and fit until one day they felt seedy and ill, and this continued until they were compelled to seek medical advice, when they were found to have a raised temperature. A few days' relief was obtained and they returned to their work still feeling far from well, and after a few weeks of the strenuous life in the trenches they collapsed, sometimes with loss of consciousness, breathlessness or even pain.

[7] The Cardiac Disabilities of Soldiers on Active Service, Lancet, London, July 22, 1916, p. 133.
[8] The Soldier's Heart, British Med. Jour., January 22, 1916, p. 117.
[9] The Irritable Heart of Soldiers, British Med. Jour., January 22, 1916, p. 119.
[10] Les tachycardiques, Arch. de mal de coeur, September, 1917, p. 408.
[11] Soldier's Heart, Lancet, London, March 24, 1917, p. 442.
[12] Loc. cit.

"The story of the onset varies. Sometimes it is an attack of diarrhea, which persists for a time; sometimes it is after a definite illness, as measles, but most give a history which we can safely surmise as being due to an infection. In a few cases one cannot get such a definite account of the starting of the illness, but many do recognize the gradual onset of the trouble. That is the story of the majority of cases, but there are a number from whom we can get no suspicious history of infection but in which there is an account of a very strenuous life."

Symptoms in Detail. Practically all observers are united in describing the same subjective and objective manifestations of the disorder, but the Research Committee's report by Lewis is so complete that it will suffice to secure a complete picture of the condition to abstract it and use it as the basis for the description of the symptomatology.

Dyspnea. This is complained of by all patients after effort; when quiet the patient does not notice it except in an occasional case of nervous, rapid breathing, but slight effort brings this out so that the respirations are increased moderately, while more severe effort will cause a rise of respiratory rate to 60 to 70 per minute.

Lewis,[13] in discussing the cause of breathlessness in patients suffering from irritable heart, expresses the opinion that it is due to the inadequate supply of buffer salts in the blood. He shows that he and his co-workers have demonstrated this, and calls attention to the fact that this symptom of breathlessness arises as a result of disordered metabolism, though the commonly accepted cause of breathlessness has been held to be instability or irritability of the central nervous system. This inadequate supply of buffer salts permits overstimulation of the respiratory center by the CO_2 developing as a result of exercise. There is an insufficiency of these salts, consequently their buffer effect is lost and the CO_2 is able to act more directly upon the center than if these salts were present to neutralize and to overcome the direct shock of the acid CO_2 upon the center.

Pain. This is another very constant symptom, occurring in over three-quarters of all cases. The pain is of different degrees, varying from slight precordial distress to severe pain over the entire precordium and transmitted down the left arm. The pain is induced by exercise. J. C. Meakins and E. B. Gunson[14] have shown that in 48 per cent. of soldiers with irritable hearts, complaining of severe pain, there is nearly always present an area of hyperalgesia over the left chest in front. This hyperalgesia is similar to that seen in cases of angina pectoris; it is increased by exertion; infection increases the precordial pain and hyperalgesia; and the presence of precordial hyperalgesia is indicative of severe cases, with poor prognosis.

Palpitation. This is also a very common symptom. In the great majority of cases it is due solely to the increased rate of the heart after exercise and disappears as soon as the heart rate slows down. Occasionally palpitation is due to extrasystoles which appear during rest to disappear during exercise.

[13] Breathlessness in Soldiers Suffering from Irritable Heart, British Med. Jour., October 14, 1916, p. 517.

[14] The Occurrence of Hyperalgesia in the Irritable Heart of Soldiers, Heart 1917, vi, 343.

Cerebral Symptoms. Vertigo occurred in about 75 per cent. of the patients. The patients were dizzy after exertion, the dizziness being accompanied by spots of light in the visual field. It was always pronounced when changing from prone to upright position quickly. This probably induced a sudden fall in intracranial pressure, though it is not always possible to show a fall; indeed, a rise in peripheral systolic pressure is seen at times.

Syncopal attacks were found to occur in six subjects. The pulse rate was slowed, though attacks did not altogether resemble those found in Adams-Stokes's disease, and the systolic blood-pressure was likewise much lowered.

Sweating and Salivation. The subjects of soldier's heart were found at rest to have moist sweating hands, and during the physical examination, sweat would run down from the axillary sweat glands. Physically effort would induce sweating out of all proportion to the degree of exercise as would a stimulation of the emotions. An increased amount of saliva was also thought to be secreted. T. F. Cotton, J. G. Slade and Thomas Lewis[15] conclude, from a series of studies upon these men after injections of pilocarpin nitrate, that "the increased activity of the sweat glands and the increased activity of the salivary glands (as estimated by the rate of swallowing) of patients suffering from "irritable heart" appear to be due to hyperexcitability of the corresponding peripheral mechanisms."

Vasomotor Symptoms. Spontaneous flushing is induced by the slightest cause. Cotton, Slade and Lewis[16] say, as a result of their studies with amyl nitrite, that this spontaneous flushing is "conditioned more often by the state of the peripheral vessels than by hyperirritability of the nervous system."

Pulse Rate. The increase of the pulse rate upon effort is one of the most characteristic symptoms found by Lewis and his co-workers. Furthermore, it is an extremely valuable objective finding in cases which may have complaints suggestive of the disorder but in whom these complaints might be due to other causes. Slow recovery of the pulse rate to what it was before exercise is a bad prognostic sign, though quick recovery is not necessarily a sign that ultimate fitness will be attained by proper treatment. J. C. Meakins and E. B. Gunson[17] show that before the simple test exercise (walk 75 paces at quick time ending in a climb of 27 steps) the average pulse rate was 86 per minute (controls 75), the rise after exercise 131 (control 110), the length of time of the return of the pulse rate to normal was in direct ratio to the severity of the symptoms. They also found that rest in bed and intercurrent acute infections have a most deleterious effect upon the return of the pulse rate to normal after exercise. John Parkman[18] found that after slight exertion and on standing the average increase in pulse rate was greater in these patients than in the controls.

[15] Observations upon Pilocarpin Nitrate, Heart, 1915–17, vi, 299.
[16] Observations upon Amyl Nitrite, Heart, 1915–17, vi, 311.
[17] The Pulse Rate after a Simple Test Exercise in Cases of Irritable Heart, Heart, 1915–17, vi, 285.
[18] The Pulse Rate on Standing and on Slight Exertion in Healthy Men and in Cases of Soldier's Heart, Heart, 1915–17, vi, 319.

Blood-pressure. The blood-pressure at rest is usually about normal. The effect of a fixed amount of exercise upon blood-pressure shows that the reaction is qualitatively the same, but the pressure rises higher and the raised pressure is longer sustained in the patients than in controls.[19]

Effect of Drugs. Digitalis, according to J. Parkman,[20] has scarcely any influence in this condition and is not indicated. Adrenalin, a sympathetic stimulator, was found to have a greater effect upon the heart sympathetic than in the normal, while apocodein, a sympathetic depressor, caused similarly a greater depression.

The Physical Examination. Aside from the pulse rate, physical examination seems to disclose but little in these cases. In fact, the absence of physical signs is one of the negative symptoms of value. In the Hampstead Hospital Report, Lewis goes into the question of systolic murmurs with considerable thoroughness. He shows that systolic murmurs *per se* have but little importance. Two hundred and sixty-six soldiers did not show any murmurs, and of these 58 per cent. were definitely unable to be restored to duty, while of 196 soldiers with systolic murmurs only 51 per cent. were unfit for duty. Meakins, Lewis and others[21] say that "A systolic murmur at the apex is not considered to be a sufficient ground for discharge, whatever the character of the murmur; in our experience many men who present this sign are capable of a great deal, if not of full and continued effort."

In these sentiments the authors are in accord with Sir James Mackenzie, who holds that the functional capacity of the heart is the criterion upon which hearts must be judged, not the presence or absence of murmurs. This view-point of Mackenzie, long held by him, but brought to the fore by his advice to medical examiners not to reject men with heart murmurs unless their hearts showed definite signs of insufficiency or gross myocardial change, precipitated an active and at times even acrimonious debate among English cardiologists and clinicians. The work of Lewis would seem to support Mackenzie's contention most completely, though the controversy still is active in English periodicals.

The Apex Beat. Extension of the apex beat downward only shows that there is hypertrophy of the heart and does not help in determining the functional capacity of the organ. Likewise the force of the beat, its definite localization or diffuseness has no value in making the above determination.

The Size of the Heart. The report of the Medical Research Committee contains some interesting roentgenological observations by Meakins and Gunson upon the change in the size of the heart after exercise. In the normal individual active exercise results in a diminution in the diameter of the heart of about 1 cm. In patients whom the exercise caused the usual symptoms a decrease in the diameter of the heart was not noted, nor was there, however, any increase in size of the transverse diameter or dilatation, though the absence of the usual and normal diminution in size might be construed as a dilatation.

[19] T. Cotton, D. L. Rapport and Thomas Lewis: After-effects of Exercise on Pulse Rate and Systolic Blood-pressure in Cases of Irritable Heart, Heart, 1915–17, vi, 269.

[20] Digitalis in Soldiers, with Cardiac Symptoms and a Frequent Pulse, Heart, 1915–17, vi, 321.

[21] Loc. cit.

Electrocardiographic Studies. These showed no variations other than occur in certain normal individuals. The tracings are of no value in diagnosis nor in prognosis.

Leukocytosis. One of the most valuable objective signs of the presence of soldier's heart is found in the leukocyte count. G. Briscoe[22] found that in cases of irritable heart there was a constant leukocytosis when the patient was up and about and increased by exercise. She found that this was slight or there was none at all during absolute rest. The degree of leukocytosis seemed to be in direct relation to the severity of the case. Thus in the 4 most severe cases clinically the counts after exercise varied between 18,000 to 23,000 as contrasted with the 4 least severe cases which showed after exercise a moderate increase, 8700 to 13,700. The rise after exercise is in all cases greater than in normal controls.

In regard to the differential count she noted a higher lymphocytic count in cases of long standing, though the highest values were obtained in a case of only six weeks' duration. The percentage rise in lymphocytes may be marked in patients who show only a slight leukocytic increase after exercise. Furthermore, the variability of the several kinds of leukocytes is greater than in normal individuals. The author also calls attention to the fact that while the leukocytosis is of value in diagnosis, being uncontrolled by the patient, in prognosis it is of not much assistance, as the condition of the blood varies with the general condition of the patient, which can be judged by the usual clinical methods.

Urine. The total quantity is usually reduced. In 60 per cent. of the cases the acidity was greatly increased. In general, amino-acids, calcium and oxalic acid are increased; phosphates and urea decreased; uric acid, creatinin, sulphates normal.

It has been suggested that the amino-acid increase might be correlated with the urea decrease as an indication of functional liver trouble.

The urinary acidity in normal controls is unchanged after exercise to increase slightly one to one and a half hours afterward, while in these subjects of soldier's heart the acidity falls after exercise to increase very much more than the normal controls in an hour to an hour and a half.

PROGNOSIS. While the present article is concerned chiefly with the symptoms and the causative factors of this condition it might be well to briefly consider Lewis's figures as to ultimate serviceability of these men: 63 per cent. of the men coming from training camps are definitely unsuitable to carry on their full duties as soldiers and but 48 per cent. when they come from active service; 64 per cent. of those who had symptoms before enlisting are unsuitable for future service; 48 per cent. are unsuitable whose first symptoms appeared at time of training and 40 per cent. whose symptoms appeared during active service. Among those who performed manual labor before entering the service, 48 per cent. and those who led a previous sedentary life 53 per cent. were unsuitable to be returned to duty. Lewis also says that the symptoms existed in 43 per cent. before enlistment, 12 per cent. developed them during the training period and 45 per cent. during active service.

TREATMENT. Detailed treatment will not be considered. Suffice it is to say that rest in bed is distinctly countra-indicated. Gradually

[22] The Leukocytes in Cases of Irritable Heart, Lancet, London, June 2, 1917, p. 832.

increasing exercise has given the best results to all observers, though A. E. Garrod[23] has called attention to a group of cases in which the myocardium is involved as a result of some fresh or recent infection and in whom exercise is counra-indicated and rest in bed indicated.

PATHOGENESIS. The pathogenesis of soldier's heart has aroused so much discussion in England, as already mentioned in the forepart of this paper, that it may be well to discuss the various hypotheses advanced to explain the condition.

I. *Blood Infection.* As recounted earlier in this paper Cotton, Lewis and Dale[24] aroused interest in the possible infectious origin of soldier's heart by describing the occurrence of an almost constant bacilluria in these cases and at times bacillemia. Subsequent work failed to confirm this, and G. Briscoe and L. Demoud[25] put at rest this theory by making 96 observations on 43 cases of irritable heart at the Hampstead Military Hospital, none of the cultures proving positive when a careful technic was evolved.

II. *Overstrain of Heart.* That sudden severe or continuous overstrain of the heart may occasion soldier's heart is a possibility in rare cases, but in the majority of cases surely there is no such possibility. Sir Clifford Allbutt[26] says that "heart strain," a phrase at one time, a few years ago, in common use, is a rare event and does not constitute the bulk of the cases invalided home as D. A. H. Thomas Lewis[27] says that the condition originated in sudden effort in only 5 cases that he had seen. Effort aggravates the symptoms and displays defects which are latent, but that it is responsible for the condition is not to be believed from present evidence. The strongest evidence of damage by strain must be forthcoming before it can be believed that so vital a muscle as the healthy heart can be injured by strain. Sir James Mackenzie says that "I never saw a single individual who suffered from heart dilatation as a result of overexertion. I think I may fairly say that this was not due to inability to recognize overstrain." In this article, in which Captain A. Abrahams[28] quotes Mackenzie, he (Abrahams) says that he has never seen a case of overstrain in the examination of many athletes' hearts. Captain J. Parkinson[29] says that among his 40 cases only 4 attributed the onset of symptoms to a particular exertion, and 3 of these cases had had recent influenza. Contrary opinions as to the likelihood of strain causing symptoms of cardiac insufficiency are held by others. Captain W. Scarisbrick[30] in his paper on the comparative incidence of heart disease among soldiers and recruits finds 26.6 per cent. of the former and 15.2 per cent. of the latter suffering with "strained hearts." Dr. I. Mackenzie,[31] however,

[23] A Variety of War Heart which Calls for Treatment by Complete Rest, Lancet, London, June 30, 1917, p. 985.

[24] Loc. cit.

[25] Bacteriological Examination of the Blood in Cases of Irritable Heart, British Med. Jour., August 18, 1917, p. 210.

[26] The Investigation of the Significance of Disorders and Diseases of the Heart in Soldiers, British Med. Jour., August 4, 1917, p. 139.

[27] Soldier's Heart, Lancet, London, March 31, 1917, p. 510.

[28] Ibid., March 24, 1917, p. 442. [29] Loc. cit.

[30] Cardiac Disease in Soldiers and Recruits, British Med. Jour., February 24, 1917, p. 254.

[31] The Soldier's Heart, Glasgow Med. Jour., 1916, lxxxvi, 213.

believes that there is no evidence to show that in cases of soldier's heart the disease has resulted from strain of a physical character. In work done before the war, Moritz, de la Camp, Selig and many other German observers claim that the heart cannot dilate under the influence of muscular tension.

III. *Hyperthyroidism.* The hypothesis that the overaction of the heart is due to oversecretion of the thyroid gland is one that appeals to many observers of the condition, nor is this view-point a surprising one when the marked similarity of the symptoms of early Graves's disease to those of the irritable heart of the soldier is considered. One of the foremost advocates of this theory in part is Dr. J. Strickland Goodall,[32] who states in his Chadwick Lecture, based on 2250 cases of soldier's heart, that many cases of soldier's heart are due to the temporary overaction of the suprarenal glands as a result of fright, with a resulting overaction of the thyroid to neutralize this stimulation of the suprarenals. The thyroid overaction persists, the suprarenals overaction is but temporary. Captain Scarisbrick[33] says that in some of his cases hyperthyroidism accounted for the cardiac neuroses. H. J. Leeuwen,[34] working under Major Tait McKenzie, found the thyroid enlarged in about 25 per cent. of his cases, and states that some of his cases suffered from hyperthyroidism. Wilson,[35] Sir James Mackenzie's assistant, says that while the theorists are bankrupt the disease remains. In 18 of his cases, however, he was interested in observing that the thyroid was enlarged and administration of thyroid caused exacerbation of the symptoms. Sir James Barr[36] says that it is no wonder that, under present conditions of war, we should get great vascular disturbance and increased function of the thyroid gland. He says that all these cases of soldier's heart depend upon an increase or decrease of the internal secretion of the thyroid and that the proper treatment in these cases is that used in the treatment of hyperthyroidism or hypothyroidism. This paper of Barr's provoked considerable discussion in the literature, pro and con, as to whether the thyroid was necessarily at fault in all cases. Dr. F. A. Stoney,[37] working at the Fulham Military Hospital, believes that there is a very close relation between hyperactivity of the thyroid gland and the tachycardia and breathlessness seen in cases of irritable heart. In addition to the rapid pulse and breathlessness, together with the sinus arrhythmia and apical systolic murmurs, there is also noted tremor, insomnia, enlargement of one or both lobes of the thyroid and, more rarely, ocular symptoms. She believes likewise that a cure may be effected by securing partial atrophy of the thyroid gland with the roentgen rays. C. P. White and F. Hernaman-Johnson[38] also contend that hyperthyroidism is the cause of soldier's heart and treatment by the roentgen rays should not be neglected.

[32] The Factors of Cardiac Irritability, Lancet, London, June 23, 1917, p. 962.
[33] Loc. cit.
[34] The Heart and Active Service, Lancet, London, September 2, 1916, p. 432.
[35] Irritable Heart of Soldiers, British Med. Jour., January 27, 1916, p. 119.
[36] The Soldier's Heart and its Relation to Thyroidism, British Med. Jour., April 15, 1916, p. 544.
[37] On the Connection between Soldier's Heart and Hyperthyroidism, Lancet, London, April 8, 1916, p. 777.
[38] Hyperthyroidism as a Cause of the Irritable Heart of the Soldier, Lancet, London, January 8, 1916, p. 78.

Among the French, Gallavardin[39] also believes that in some cases the thyroid may be at fault, though this explains only some of the cases. D. Pletnew,[40] on the contrary, says that he has almost never seen it. Lewis[41] summarizes the opinions against incriminating the thyroid as follows: In spite of the frequency with which the thyroid is said to be enlarged by advocates of the hyperthyroid hypothesis, in his series of cases only 4 per cent. showed this sign; the symptoms of tachycardia, tremor and so on are seen after infectious diseases, and the thyroid is not asked to explain them; roentgenotherapy gives too doubtful results to be good evidence; and finally thyroid extract given experimentally seems to have no more effect on these cases than on other unrelated cases.

IV. *Disturbance of Nervous System.* All authors agree that the nervous element plays a more or less important part as an excitant of the disorder. Mental stress is if not a greater at least an equal factor with physical stress in exciting the attack. Some writers claim it is the entire and sole cause. For example, Dr. I. Mackenzie[42] says that the soldier's heart in all probability belongs to the disorders of psychic origin. Tullidge[43] also calls attention to the psychic origin of the neuroses. R. D. Rudolf[44] says that "the condition is in reality part of a general nervous instability—in other words, neurasthenia." Dr. Poynton[45] believes that nerve shock is a factor of importance in some cases. Alexander Morrison,[46] in discussing the question as to the pathogenesis of the condition, says that in his belief the condition is one of neurasthenia or psychasthenia. Sir William Evart[47] holds that the heart may collapse as a result of gradual exhaustion of the myocardium, myocardial failure or as a result of some overwhelming shock in a nerve-worn subject, functional heart stroke, and that "soldier's heart" is probably a combination of these two factors.

Lewis discusses the hypothesis of the nervous system causing the condition in brief as follows: In general the subjects of cardiac irritability are emotional, high-strung individuals with exaggerated reflexes. Vagal tone is not abolished, as experiments with atropin show, but that the vagus action is normal is questionable because the pulse fails to return to normal after exercise, because sinus (vagal) arrhythmia is often exaggerated in many cases and because syncopal attacks with extreme slowness of heart occur in some cases. On the other hand, lack of vagal tone does not appear to be responsible in irritable hearts, for the high pulse rate or the exaggerated response to exercise, rather a hyperirritability of some portion of the system which includes the acceleration reflex arc and the rhythm-producing center itself. Experiments with adrenalin and apocodein show that the sympathetic system is more easily stimulated or depressed than normal in those individuals

[39] Loc. cit.

[40] Insuffícance cardiovasculaire . . . . de la guerre, Arch. de mal de coeur, 1916, ix, 333.

[41] Loc. cit.

[42] Loc. cit.

[43] The Heart of the Recruit and the Soldier, Military Surgeon, 1917, xl, 24.

[44] The Irritable Heart of Soldiers, Canadian Med. Jour., 1916, vi, 796.

[45] British Med. Jour., January 22, 1916, p. 130.

[46] Ibid., 1911, p. 184.

[47] The Soldier's Heart and the Strained Heart, British Med. Jour., February 5, 1916, p. 218.

suffering with irritable hearts. In all probability these variations in nervous excitability are secondary to changes in cellular metabolism or to true intoxications.

V. *Myocardial Lesions.* At the Hampstead Hospital it is the custom to sift out all cases of frank valvular and of myocardial diseases, referred there as D. A. H., before listing the remaining cases as having irritable hearts. In spite of this many of the cases of the irritable heart of soldiers gave a history of previous rheumatism or chorea, suggesting that mild myocardial lesions may give rise to the symptoms. Autopsy alone would be able to verify this. The electrocardiogram was unable to show any such evidence of myocardial disease in 10 cases examined by Parkinson. It does seem, however, hard to conceive of acute rheumatic fever leaving the heart muscle untouched, and it would seem that in these cases at least the myocardium was involved. Parkinson[48] in his study of 40 cases of soldier's heart excluded frankly diseased hearts. He believes that the relative cardiac insufficiency may be a sequel to certain acute infections, may be the result of myocardial changes due to age, may be associated with functional nervous disorders and may be due to endowment with a heart of limited efficiency. Garrod[49] calls attention to the fact, also, that there are certain cases of soldier's heart, following immediately after acute infections, in whom "the myocardium is damaged for a time." He concludes his article by saying that "the soldier's heart is not a clinical entity but includes a variety of morbid states."

Another phase of the question of the heart itself may be here considered, that is, the heart that is distorted in position or hypoplastic. Goodall[50] says that hearts showing persistent overexcitability of muscle or nerve are too horizontal in position because they are too soft. This lack of tone may be the result of impaired nervous control, habitual overwork with insufficient rest, or disuse, insufficient use or misuse. D. Pletnew,[51] in concluding his article on cardiovascular insufficiency in the war, says that the greatest number of soldiers who present the phenomena of cardiovascular insufficiency are individuals in whom early arteriosclerosis is appearing or whose heart and aorta are hypoplastic. In addition to insufficient development of these organs the disharmonious development of the different organs, plays an important part in the pathogenesis of insufficient heart. This latter develops most frequently among well-built men who have not been accustomed to muscular exercise. It might be added here that many of the English authors also call attention to the necessity of starting military training with mild exercise gradually increased.

VI. *Toxemia.* The hypothesis that a toxemia is the agent responsible for the disorder is the one accepted by Lewis as seemingly the most feasible. Receiving as it does the approval of Mackenzie[52] and Allbutt, as well as Lewis and his co-workers, who have studied the question so carefully from all angles, it is needless to state the hypothesis that is most generally accepted both in England and France.

[48] Loc. cit.
[49] A Variety of War Heart, Lancet, London, June 30, 1917, p. 984.
[50] Loc. cit.
[51] Loc. cit.
[52] The Soldier's Heart, British Med. Jour., January 22, 1916, p. 117.

This hypothesis is based on the following facts: Most of the cases started from some infection; the symptoms are analogous to those appearing in convalescence from acute infections or in the early stages of pulmonary tuberculosis; the changes of the urine and of the blood, mentioned in the forepart of this paper, suggest an infection. This hypothesis assumes either the production of true toxic bodies acting on the heart or disorders of cellular metabolism resulting from the infectious process.

In closing this discussion of irritable heart it might be appropriate to insert here, while considering the toxic hypothesis, some remarks Sir Clifford Allbutt[53] made upon the researches of Dr. Lewis and his associates at Hampstead Hospital: "Setting aside for the while poisoning of the myocardium, may incidental infections produce any other effects in which the heart is concerned? The answer appears to be in the affirmative. These researches seem to discover a new disease, or rather to discriminate more exactly the features and nature of a disease less clearly apprehended already, by Da Costa and others as soldier's heart; or by those of us who have written upon neurasthenia as cardiac neurasthenia. The disease is one which is not uncommon in the civil population, but under the stress of the soldiers' training and among the aggregations of men in modern armies, it is more conspicuous and inconvenient."

Classification of Tachycardias Used in Examination of the Soldiers of the Thirty-eighth Division. Before discussing the classification of the large number of cases of tachycardia seen during the course of the cardiovascular examination at Camp Shelby, it may be well to sketch briefly the method of procedure in making the cardiovascular examinations. The cardiovascular examiner worked in conjunction with the tuberculosis board which examined practically every man in the command. The several members of this board in examining the thorax would percuss and auscult the heart at the same time they were going over the lungs. Any abnormality that they might detect in the heart, such as abnormalities in the cardiac impulse, excessive rapidity or slowness, murmurs, irregularity, accentuations and enlargements, was sufficient to refer the individual with the abnormal condition to the cardiovascular examiner. When a man was referred for cardiovascular examination a note was sent with him stating for what reasons he was referred. The examiner working alone in a separate room of the regimental infirmary then went over the soldier carefully and studied the condition thoroughly in order to determine the effect that it might have upon the soldier under the stress of active campaigning.

In addition to the usual methods of physical examination the functional strength of the heart was estimated by having the examinee hop seventy times on one foot. The pulse was counted before the hopping test, immediately afterward and two minutes later. A return of the heart rate preceding exercise, provided that immediately following exercise there was an increase in rate, was considered evidence of good functional capacity of the organ. In reference to this exercise test of functional sufficiency of the heart, which is recommended by the

[53] Loc. cit.

Surgeon-General's Office and which is generally considered the best test of cardiac sufficiency, it might be well to quote Meakins, Lewis and others.[54] "It has been our special endeavor to find some relatively simple and quick test which will eliminate the unfit, and for this purpose we have made elaborate observations upon pulse rate, blood-pressure and respiratory rate under various conditions of posture and exercise. We have taken numerous instrumental records, polygraphic and electrocardiographic; we have also noted such physical signs as basal murmurs, jerky impulse, extended impulse, various alterations of the heart sounds and signs of vasomotor instability; with a solitary exception we find these to be of no value in gauging the grade of exercise which will be ultimately tolerated or readily be borne. The solitary exception is the rate at which the pulse falls when it is accelerated by a brief exercise." C. Lian,[55] in France, is also an advocate of this method of testing the functional efficiency of the heart while in this country. T. B. Barringer, Jr.,[56] has done a great deal of work upon this same principle.

Nine hundred and forty-four soldiers, from the division of a strength of 22,622 at the time of the examination, were sent for special study of the cardiac condition. Of those thus referred, 424 (44.9 per cent.) were sent with the diagnosis of "tachycardia." It is thus seen that a very large number of the cases studied were cases of a rapid heart action. In fact, the provisional diagnosis of tachycardia exceeded by a large number any other single diagnosis. The heart rate was determined by counting the number of systoles heard by the stethoscope over the precordium in thirty seconds. The cardiovascular examiner was authorized by the Surgeon-General to act upon these cases in three ways, either unconditionally to "reject" or to "accept" the examinee as a soldier, or to "accept conditionally," with the idea that a future examination would show if the condition had so improved under training that the man could carry on the duties of a soldier.

In the study of the 424 cases of tachycardia seen at Camp Shelly it was obvious that an opportunity was afforded of classifying these possible future cases of soldier's heart before the actual onset of the trouble. In other words, an etiological factor might be determined ante rather than post, as was necessary in the English studies. Furthermore, by classifying these subjects with rapid heart it would be possible more satisfactorily to dispose of them in one of the three ways recommended by the Surgeon-General's Office, namely, accept, reject or accept conditionally. One may rightly judge, from the various hypotheses concerning the pathogenesis of soldier's heart discussed in the forepart of this paper, that there is still considerable haze as to the true factor in the production of the disorder. In spite of Lewis's masterly work there still seems, for example, a strong possibility that the thyroid may be implicated in a certain number of cases. Likewise it seems quite definitely proved that soldier's heart, while excited by an infection,

[54] Loc. cit.

[55] Épreuve d'aptitude cardique a l'effort, Presse méd., December 7, 1916, p. 563.

[56] The Circulatory Reaction to Graduated Work as a Test of the Heart's Functional Capacity, Arch. Int. Med., 1916, xvii, 363. Also, Studies of the Heart's Functional Capacity, Arch. Int. Med., 1917, xx, 829.

is predisposed to by certain factors. The work of the English has all been done upon cases already the subject of soldier's irritable heart. There the predisposing or etiological factor had to be determined after the onset of the trouble, whereas in the present study it could be determined possibly before the trouble appeared, but as the question of the pathogenesis is still somewhat in doubt it was thought wise to classify these cases of tachycardia not from one view-point alone but to make a classification which would combine the best of the ideas as to the cause of "soldier's heart." Many of the cases of tachycardia that were seen during the course of the examinations seemed unlikely to develop "soldier's heart" and could be grouped in other classes.

The following five etiological classifications of the tachycardias were made: (1) Myocardial. (2) Hyperthyroid. (3) Neurotic. (4) Nervous (emotional). (5) Toxic.

These groups will be completely discussed seriatim, giving the number of cases in each group, their findings at the time of the examinations, the reason for classifying them in such a manner and their dispositions.

The first three groups represent cases that may develop "soldier's heart," the last two represent tachycardia of mild degree in whom it is believed no such result will obtain. These last groups will be discussed in the light of the experience of others more fully than the first three groups, which have been dwelt upon from this view-point in the early part of the paper.

1. *Myocardial.* Sixty-nine cases, or 16.3 per cent., of the tachycardias were of this type. The diagnosis was based upon the history of the individual, the physical findings and the functional tests. In considering the history, and it is in the individual with this type of rapid heart that the history is most important, it was noted that a large majority of these soldiers had suffered from pneumonia some time during the preceding five years, an interesting commentary upon the deleterious effect of pneumonia upon the heart. The present history was also important. The soldier suffered from dyspnea upon slight exertion, a cough was sometimes present and there were other subjective evidences of a very moderate degree of cardiac insufficiency. The physical examination, outside of the tachycardia, usually showed but little. At times a slight enlargement of percussion dulness was noted.[57] The functional test, the response to exercise was also of great value in determining this type of tachycardia. Failure of the pulse to return to normal within two minutes was considered an evidence of myocardial weakness and was the *sine qua non* in diagnosing these cases.

The disposition of the soldier with a rapid heart, presumably the result of myocardial change of a moderate degree such as outlined above, was usually "accept," as it was felt that the gradually increasing exercises of the training period would materially benefit the heart so

[57] It should be understood that frank cases of myocardial disease and cases of valvular heart disease with associated myocardial weakness were not listed in this group. These cases were diagnosed "myocarditis, chronic" and "valvular heart disease," and as such were considered. The above classification includes only those cases that are questionable. The term myocardial tachycardia is used because of the apparent slight degree of myocardial involvement. There was a history of pneumonia and there was a myocardial insufficiency, but that there was a true pathological myocarditis which could be demonstrable at autopsy could not be proved.

that he would be able to go through hardships of any type. Cases giving a history of acute rheumatic fever were rejected, as it is almost impossible to imagine the myocardium not being injured after this disease. Furthermore, Lewis found a large percentage (about 20 per cent.) of his cases of soldier's heart gave a past history of this disease.

2. *Hyperthyroid.* Ninety-seven cases of tachycardia attributable to malfunctioning of the thyroid, or larval hyperthyroidism, were seen. Three symptoms of hyperthyroidism were considered necessary to place a man in this group. Two of these symptoms were practically constant, a pulse rate of over 130 and a fine tremor; the third symptom was either enlargement of the thyroid or well-marked vasomotor symptoms. Exophthalmos was seen only a few times. The response to the functional test was usually poor. These cases were usually fairly easy to determine. Their disposition was, excepting in the well-marked unquestionable cases, which were rejected, generally "provisionally accept," as it seemed likely that these men would probably break down under the stress of trench warfare, developing exophthalmic goitre if not soldier's heart. If upon subsequent examination the symptoms have not disappeared it would seem wise to discharge them upon a surgeon's certificate of disability. An interesting point in regard to these cases was that a large percentage of them were found in a regiment recruited in the mountains of West Virginia. In this same regiment there were also found many men with symptomless goitres.

3. *Neurotic.* In this group fell the largest number of cases, 180 (or 42.5 per cent.). These men practically all presented the following syndrome: A pulse rate of over 120; an exaggerated sinus arrhythmia, and a functional heart murmur, systolic in tone, soft and blowing, heard best over the second and third interspaces, referred upward and to the subclavian artery, and never to the axilla. In discussing the murmur systolic in time, heard over the pulmonary valve area, H. M. Raven[58] says that in his experience with a camp of over 2000 boys under nineteen, a large number of them have this murmur. It is associated with poor physique and retarded development. He suggests that in addition to the commonly accepted theory that it arises as a result of friction between the pulmonary artery and the chest wall or adjacent structures, another theory might be advanced, that it is due to a relative or actual narrowing of the pulmonary artery (congenital). In these cases D. A. H. symptoms are very common.

The term neurotic is poor but was employed because these men all had many and diverse complaints of all kinds. Their subjective symptoms were pronounced, not only symptoms referable to the heart but symptoms which were indefinite, vague and uncertain, and referable to all parts of the body. Vagal might perhaps be a more satisfactory term, as they showed usually pronounced evidences of vagus instability. The majority of these men were listed as "conditionally accept." The experience of the English has shown that men falling into this classification are unable to stand the wear and tear and stress of severe campaigning. It is from this group that will probably come the most men who will develop the irritable hearts of soldiers. Their symptoms, their vagal instability, their heart examination, their rapid pulse rate,

[58] British Med. Jour., August 25, 1917, p. 251.

their poor response to the functional exercise test, all these findings are characteristic of the typical case of "soldier's heart." Indeed, they might readily be said to belong to that large class mentioned by Lewis in whom symptoms appeared before enlistment and who are not truly subjects of "soldier's heart," in the sense that the soldier's life is necessary to cause "soldier's heart." Some mild infection incurred before ever seeing active warfare may so exaggerate the symptoms that the man is no longer fit for active soldiering. It would be interesting to see how well these men respond to the splendid hygiene of camp life. Probably a goodly number will be so immeasurably benefited by the exercise, outdoor life, proper food, regular hours and careful life of camp that they will be able to go through with any future assignments they might receive. In the meantime by listing them as "conditionally accept" they will be under constant observation, and should they not be materially benefited by their new environment, should be kept in this country to perform military duties less arduous than those they will meet with overseas.

4. *Nervous (Emotional).* The soldiers with rapid hearts who fell into this classification presented few objective or subjective manifestations of disordered heart. The tachycardia was not excessive, rarely over 120, physical findings were negative and the response to the functional test was normal. There were only twenty-eight men referred who were listed in this group. This may seem like a surprisingly small number, but it is small because such a diagnosis was made only when the pulse rate was unduly rapid. The men with the slower pulses were listed as "heart normal." The men of this group if allowed to sit quietly for twenty or thirty minutes to watch the examinations going on, in order to do away with the nervous excitement incident to the examination, and then examine them, their hearts would be found to have normal rates.

Two opinions as to the relatively innocuousness of this type of tachycardia may be mentioned. Sir James Mackenzie[59] calls attention in his brief memorandum to medical examiners to the effects of excitement. He states that many candidates with perfectly healthy hearts suffer from excited action of the heart during examination. The heart becomes rapid but soon slows down if the candidate lies down and breathes slowly and deeply for a few minutes. Such a candidate is considered suitable for enlistment if there is a history of good functional efficiency. A. Morrison[60] is in complete accord with the idea that "the augmented and accelerated action of the emotional heart ought also to lead to few rejections."

5. *Toxic.* Thirty-six cases of tachycardia, apparently due to intoxication of some kind, are grouped here. Some of these men were suffering from tonsillitis or some other mild infection at the time of the examination. Some were smoking an excessive number of cigarettes a day—thirty to sixty. Some few were alcoholic. Some were drinking enormous quantities of coffee. All of them had a rapid heart, apparently the result of some toxin, whether bacterial or a drug. Cases of tuberculosis or other severe infection with the associated tachycardia are

[59] The Recruit's Heart, British Med. Jour., October 16, 1915, p. 563.
[60] Ibid., October 30, 1915, p. 636.

not grouped here. Except for the rapid heart, physical examination disclosed nothing of moment. As regards effects of cigarette-smoking and alcohol there is of course considerable divergence of opinion.

Cigarette-smoking undoubtedly has the effect of increasing the heart action, but that it has any more serious effect is dubious. J. Parkinson and H. Koefid,[61] in a recent article in which the effect of cigarette-smoking is fully discussed, conclude that the smoking of a cigarette by habitual smokers raises the pulse rate, which effect is more pronounced in cases of soldier's heart; that excessive smoking is not the essential cause in most cases, but in their opinion it is an important contributory factor in the breathlessness and precordial pain of many of them. R. D. Rudolf[62] says that the excessive use of tobacco is often stated to be a cause of soldier's heart, and no doubt in many cases it is one. Lewis, however, does not lay much stress on tobacco as a cause of disordered action of the heart. In his series 5 pe · cent. did not smoke, and he calls attention to the fact that the same symptoms appear in soldiers who do not smoke. Likewise with alcohol, more than half of his cases were not consumers of alcoholic drinks and many of them showed actual distaste for it. Parkinson[63] found in his series of 40 cases that about half either smoked a pipe or were very light smokers, and that in regard to alcohol only 3 had been heavy drinkers. E. K. Tullidge[64] in his experience in Austrian service says that in a number of cases the disturbance could be traced directly to the excessive use of tobacco.

Fourteen cases of rapid hearts were seen which fell into no category. It was apparently impossible to group them satisfactorily.

SUMMARY. "Soldier's heart" is discussed in the light of the experience of our allies. The importance of tachycardia as a prominent and important objective symptom in the examination of the recruit is called attention to and a classification for cases of tachycardia is suggested.

NECROPSY SERVICE IN A MILITARY HOSPITAL IN THE FIELD.

By HOWARD T. KARSNER, M.D.,
CAPTAIN, M. R. C., U. S. ARMY, FRANCE.

THE following report is offered not because of its statistical value but because it represents fairly well the type of work a pathologist sees in a base hospital in France and because it offers certain suggestions as to the sequences and treatment of war wounds. It represents eight months' service in a base hospital in France of about 1250 beds. The total number of necropsies is 87, which represents nearly all the deaths that occurred in the period mentioned. The necropsies were performed under fairly satisfactory conditions, and, as a rule, a few hours after death. There were no limits as to the extent of the examination,

[61] The Immediate Effect of Cigarette Smoking on Healthy Men and on Cases of Soldier's Heart, Lancet, London, August 18, 1917, p. 232.
[62] Canadian Med. Assn. Jour., 1916, vi, 796. [63] Loc. cit.
[64] The Heart of the Recruit and the Soldier, Military Surgeon, 1917, xl, 24.

and bacteriological examinations were made in all cases. The finer differentiation of bacteria was not possible because of limitations of time and staff. The study of anaërobes was difficult, and the results given are to be regarded as approximations rather than as accurate diagnoses of the anaërobes. For this purpose the primary culture was made in a medium recommended by Hibler and by Muriel Robertson, composed of lean beef, and water, equal parts, rendered slightly alkaline to litmus, tubed and autoclaved. A final estimation of the cause of death was not possible in some of the more complicated cases, and the cause assigned was that dictated by a consideration of the clinical and pathological aspects of the case.

Probably the most important phase of this report is the problem of dissemination of infection. Most of the war wounds contain several different organisms, and there appeared to be no explanation for the fact that in some cases the anaërobes are the most important for the patient, and that in other cases different forms of aërobes do the most damage. There were 28 cases in which streptococci were isolated from the heart's blood after death. Of these 2 were regarded as streptococcus pyemias, meaning metastatic suppurations in more than one position. The remainder are regarded as septicemias, although not all of them showed clinical symptoms. The technic of the heart cultures was very carefully controlled, and there is little likelihood that the organisms were contaminations; but there is always to be considered the possibility that they may have entered during the agony or after death. The cultures were pure except for 2 cases, in which Staphylococcus pyogenes aureus was also present and 5 in which an anaërobe was present as the result of gas gangrene, 4 being perfringens and 1 a motile organism, probably malignant edema. Only 1 case, a buttock wound, showed a demonstrable thrombophlebitis. Ten were cases of deep muscle wounds sometimes associated with bone injuries. Three followed penetrating head wounds, 3 penetrating pelvis wounds, 4 penetrating chest wounds and 9 followed wounds of the joints. Of these last 5 were of the knee-joint alone, 1 of knee and ankle, 1 of knee and elbow, 1 of hip alone and 1 of ankle alone. The seriousness of wounds involving the joints has been repeatedly emphasized by the surgeons, and much has been said and written about their treatment. This study can present no figures as to the frequency of septicemia as a complication, but does serve to draw attention to its importance, and any consideration of treatment must include this possibility. Attempts to save members, the joints of which are the seat of infection, must be most carefully guarded by close study of the case, and refractory cases should be subjected to most radical treatment, preferably amputation. There were 2 cases of pyemia due to Streptococcus pyogenes, 1 with large wound of buttock, fibrinous pleurisy and septic infarcts of the lungs and acute tricuspid valvulitis, 1 with penetrating wound of the pelvis, acute fibrinous pleurisy and septic infarcts of the lungs.

There were 7 cases in which Staphylococcus pyogenes aureus was isolated from the heart's blood; 3 of these were pyemias and 4 septicemias. In none of these were there wounds of joints, although 2 of the septicemias originated in chest wounds and 1 each of the pyemias and septicemias originated in penetrating wounds of the pelvis.

In addition to these septic cases there were 2 which were clinically and pathologically septicemic, but which were not identified bacteriologically because of faulty technic. There was 1 case of acute purulent meningitis due to Streptococcus pyogenes and apparently metastatic from an arm wound, although there was no growth in cultures from the heart's blood. Thirteen of the septic cases showed an acute valvular endocarditis; this matter, however, will be made the subject of a separate report. Of the 37 septic cases 27 showed spleens that were more than 150 grams in weight. There were 14 cases in which the liver weighed more than 2000 grams; 2 of these were not associated with enlargement of the spleen. The kidneys together weighed more than 300 grams in 21 cases, in 19 of which there was associated enlargement of the liver and spleen and in 2 there was associated enlargement of the liver only. Of the 37 cases only 5 failed to show parenchymatous change in the liver or kidneys or acute splenic hyperplasia. Of these 5 cases 4 were bacteriologically streptococcus septicemias and 1 was classed as a pyemia on the basis of gross morbid anatomy, but without bacteriological proof.

There were 17 cases of gas gangrene. Two of these died before the laboratory was equipped for satisfactory anaërobic work. Of the remaining 15 the heart's blood contained in 8 cases Bacillus welchii, in 2 cases a motile organism, believed to be the bacillus of malignant edema, and in 5 cases there was no growth. Of the cases showing organisms in the blood, the blood and tissues showed the usual foamy characters in all but one instance. Of the 5 showing no growth the organs and blood showed foamy change in 2 cases. In a general way it may be said that the cases reported "no growth" were sectioned earlier than those showing organisms, but one of the malignant edema cases was sectioned four hours after death and showed foamy organs. Most of the wounds were large deep wounds, 9 cases being thigh wounds, 3 of buttocks and pelvis (only one penetrating the gut), 3 arm and shoulder, 1 of the foot and 1 following an appendectomy; 5 of the cases were accompanied by a streptococccus septicemia. There are no particular notes to be made on the gross morbid anatomy of these cases, as the changes are well known and are modified in the usual way by the atmospheric temperature and the number of hours elapsed between death and autopsy. The cases were ill from three to fourteen days, the average being seven days. The average is raised by 2 twelve-day and 1 fourteen-day case, 4 being sick seven days and 7 being sick five days or less.

There were 12 cases of penetrating wounds of the chest. Most of these were studied bacteriologically before death by daily punctures of the chest. Frequently such punctures were sterile until four or five days after the wound had been inflicted, and such findings are common also in the non-fatal cases. Two of the cases should properly be classed as deaths from hemorrhage, one a hemorrhage into the chest following evacuation of a large amount of blood from the chest, the other showing frequent hemoptysis from a perforation of a branch of the pulmonary vein about 3 mm. in caliber. All but 2 cases showed a marked pleurisy, the 2 exceptions being cases of extensive old fibrous adhesive pleurisy, and 1 of these was a case that died of hemoptysis. Of the other 10 cases which showed acute pleurisy 9 had a bilateral involvement; 1 case showed also acute serofibrinous pericarditis; 5 cases had pene-

trating wounds of the lung and a bronchopneumonia; 1 of these showed also a most extensive acute interstitial pneumonia. Of the 7 cases without penetration of the lungs, 5 showed bronchopneumonia; 2 cases showed streptococcus in the heart's blood and 1 showed Staphylococcus pyogenes aureus. The fluid in the chests frequently showed the common wound flora, and a smear of the fluid, as a rule, could not be differentiated from a smear from a large superficial wound. In 1 of the cases Bacillus welchii was found in the heart's blood, although there was no foam in the blood and no evidence of gas gangrene. Most of these cases were ill about a week, but 1 was ill sixteen days, 1 ill twenty-one days and 1 ill twenty-seven days. The last showed a staphylococcus septicemia. The 2 streptococcus septicemias were ill nine and ten days respectively.

There were 9 cases of penetrating wounds of the head. These were all cases with penetration of the dura, but varied from cases with penetration of small pieces of shell or shrapnel to massive brain injuries with 3 cases of hernia cerebri. Six cases showed acute purulent basal meningitis, in 2 of which there was extension to the spinal meninges. In 3 of these cases, including the 2 with spinal involvement, there was pus in the ventricles. One other case showed an acute internal hydrocephalus associated with thrombosis of the lateral sinus, but no other evidence of infection. One case with basal meningitis and large wound of brain (tank rivet) showed extensive hemorrhage into the ventricles. Two cases died apparently of extensive subdural hemorrhage without real evidence of infection. None of the cases showed a septicemia. Five of the cases had been ill from two to nine days; 1 was ill twenty-eight days and died of meningitis; 1 was ill thirty-seven days and died of acute internal hydrocephalus; 2 cases which died respectively of brain abscess and meningitis lived forty and forty-five days.

There were 3 cases of penetrating wound of the spine. In one of these (sick nine days) there was fracture of the third lumbar vertebra, with hemorrhage in the pia arachnoid, but no suppuration. There was paralysis and anesthesia of the right leg and incontinence of retention, with acute hemorrhagic cystitis. Another case was sick four days and showed a shrapnel fragment embedded in the fourth thoracic vertebral body, severing the cord almost completely, with slight local purulent meningitis; there was a paraplegia and a most severe hemorrhagic cystitis. The third case, which lived twenty days, showed a small free shell fragment at the tenth thoracic region, with a profuse purulent inflammation of the membranes of the cord, the entire brain and the ventricles of the brain. There was no paralysis and no cystitis. None of the cases showed a septicemia, although the last case had had streptococci in his spinal fluid for more than ten days.

There were 9 cases of death apparently from hemorrhage; 6 of these had had more than 1 hemorrhage. Three of the latter group were chest wounds with penetration of the lung, one showing in addition a streptococcus septicemia. Of the 6 other cases the hemorrhage followed a wound of the pelvis in 1 and wounds of the lower extremity in 5 others; 2 of these 6 cases showed a streptococcus septicemia; 4 had been transfused without reaction, 2 cases once each, 1 case twice and 1 case three times. Of the total of 9 cases the spleen was enlarged in only 3, 2 of these having had a single transfusion, the other having had no transfusion but being a subject of a streptococcus septicemia. The bone

marrow was normal. The case which had had two transfusions had been sick twelve days, was a streptococcus septicemia and had a spleen slightly enlarged (180 grams), but otherwise normal. The case which had had three transfusions had been ill sixty-nine days with an enormous buttock wound, was not septicemic and showed a soft spleen weighing 120 grams. The general results found in this series of cases was to the effect that transfusion with matched bloods shows little effect from the view-point of gross morbid anatomy. From the clinical and pathological observations it was decided that wounds of deep vessels in the thigh and about the knee were often so obscured by the depth and the infection and the irregularity of the wound that unless the hemorrhage after careful dissection and examination could be completely stopped the surgeon must consider the advisability of amputation for the purpose of controlling the bleeding. In civil surgery this might seem extremely radical, but the conditions of military surgery sometimes make it necessary.

In addition to the 9 foregoing cases of hemorrhage there were 3 of hemorrhage complicated by transfusion reactions. The first was a shell wound of the pelvis with repeated hemorrhage, which after a transfusion developed chills and cyanosis and died in a few hours. There was no hemoglobinuria, and the spleen aside from weight (160 grams) appeared to be normal. The second case had two transfusions following a single large hemorrhage from a shell wound of the pelvis, the second transfusion through a confusion of names resulting in the use of a group 2 donor for a group 4 recipient. At necropsy there was found a firm enlarged spleen (360 grams) hemoglobinuria, normal bone marrow and a streptococcus septicemia. The third case had 1 transfusion for a large hemorrhage from a shell wound involving the popliteal artery; there was immediate reaction followed in a few hours by death, and it was afterward found that a group 3 donor had been used for a group 2 recipient. There was no hemoglobinuria and the bone marrow was normal, but the spleen weighed 170 grams, was tense and showed numerous small hemorrhagic infarcts. This patient had been ill for twenty days and was clinically a case of septicemia, but cultures from the heart's blood at autopsy showed no growth.

There were 4 deaths following "mustard-gas" poisoning, an extremely irritant gas $(CH_2)_4Cl_2S$, which was first used by the German army in the summer of 1917. One of these showed a mild bronchopneumonia and suffered also from a Staphylococcus aureus septicemia following a shell wound of the pelvis. The other 3 cases had no wounds. They all showed skin burns of varying degree. The necropsies showed a dusky red congestion of all the viscera, including in 2 cases the brain, accompanied in the stomach by submucous petechiæ in the fundus. The conjunctiva and the membranes of the nose and pharynx were the seat of a marked mucous inflammation. The larynx, trachea and bronchi showed severe inflammation, in 1 case accompanied by pseudomembrane formatiom and in the other 2 with extensive necrosis of the mucosa, with multiple ulcers from 1 to 3 mm. in diameter. Two of the three showed acute fibrinous pleurisy. All showed a bilateral bronchopneumonia, with slight general edema of the lungs. The pneumonic patches were irregularly distributed, and varied in size from

2 mm. to 3 cm. in diameter, reddish gray or gray in color, solid, projecting in the cut surface, moist but finely granular.

Of the miscellaneous cases not justifying special description were 1 each of multiple pulmonary embolism, fat embolism, diabetes mellitus, malignant endocarditis (non-surgical), insufflation pneumonia following a traumatic tracheo-esophageal fistula, acute dilatation of the stomach in a case of congenital aplasia of the jejunum, ileum and colon.

It will be noted that in the eight months' service, from May 25 to January 25, there were no deaths from lobar pneumonia, although bronchitis and bronchopneumonia were of very frequent occurrence. There was no case of active pulmonary tuberculosis, although 10 cases showed the so-called healed lesions, small caseous or calcified areas surrounded by fibrous connective tissue. In addition to these cases there were 18 cases of chronic adhesive pleurisy without any evidence of tuberculosis to the ordinary careful gross examination. Of these, 10 were apical adhesions, 4 basal and 4 extensive, involving practically the entire pleura.

In passing from civil life to work in an active military hospital in the field the medical officer is beset by many difficulties and must readjust his point of view in regard to many things. The above series of necropsies was found to be of value in several respects. The results served to alter the surgical treatment of wounds of the extremities, particularly those involving joints to a considerable degree. In place of the conservative surgery of civil life which permitted in the badly infected war wounds the possibility of a septicemia, with its incident effects on internal viscera, there developed a more radical surgery which, although it might sacrifice a limb, assured the patient of survival with little chance of damage to important viscera. In regard to hemorrhage the postmortem examination of wounds showed the possibility of large vessels being wounded in such a way as to escape detection even with most careful operative dissection. This led to several amputations for the complete control of hemorrhage, undoubtedly to the advantage of the patients. Deaths from transfusion with antagonistic blood, which the necropsy showed to be largely due to the transfusion reaction and not to other causes, led to a firmer insistence on careful testing of the bloods before transfusion. It is believed that this is even more important, if possible, at the base where patients may have been drained by infection for days or weeks than in the hospitals near the front, as has been indicated in another paper.[1] The accurate diagnosis of cases permitted by postmortem examinations is undoubtedly an aid in the adjustment of pension and insurance claims as well as statistical value in the army medical service. With all these points in view it is urged that postmortem examinations should be established as a routine procedure because of their unquestioned value to the soldier, to the army and to the nation.

[1] Jour. Am. Med. Assn., 1918, lxx, No. 77, p. 769.

REVIEWS

MEDICAL WAR MANUAL, No. 2. NOTES FOR ARMY MEDICAL OFFICERS. By LIEUT.-COL. T. H. GOODWIN, R. A. M. C. Pp. 112; 33 illustrations. Philadelphia and New York: Lea & Febiger.

ANY American medical officer who fails to read this little book neglects an opportunity to add to his efficiency. The distinguished author of this manual, Colonel Goodwin, of the British Royal Army Medical Corps, understands the medical problems of the European battlefields as few men do. In the brief compass of this book he has summarized his long experience at the front and has answered most of the troublesome questions that confront every American medical officer anticipating active duty with our troops in France.

The book is divided into three sections: The first part deals with the organization of the British medical service and the duties performed by its various officers and units. A useful comparison has been drawn between our own medical department and that of our English ally. The chapter furnishes a definite idea of just what is required of medical officers from the battalion surgeon, serving with troops in the trenches, back to the large groups of specialists working in the stationary hospitals in the rear.

The second part of the book takes up war surgery. Obviously it would be impossible in a work of this type to treat so broad a subject exhaustively. Colonel Goodwin's object evidently has been to emphasize the salient points, the fundamental principles that must never be lost sight of if the wounded are to be successfully handled. He has attained his purpose. To read this chapter is to have one's perspective properly adjusted so as to see more clearly the essential difference that exists between civil and military surgery. The account of the emergency handling of fractures is especially noteworthy.

The concluding section of the book on sanitation in war is of unusual interest and importance. In it the author discusses such vital problems as the disposal of excreta and waste in the zone of the advance, the protection of water supplies, the destruction of lice and flies, the management of divisional baths, the disinfection of clothing, and the control of infectious diseases.

From cover to cover the book is full of valuable information, presented with unusual interest, and arranged in a convenient form for ready reference. Like all the war manuals in this series its size admits of the book being easily carried in the pocket of any uniform. It is decidedly the most generally useful work of its kind that has appeared and it undoubtedly deserves a place in the armamentarium of every medical officer. G. M. P.

MILITARY OPHTHALMIC SURGERY. By ALLEN GREENWOOD, M.D., GEORGE E. DE SCHWEINITZ, M.D., and WALTER R. PARKER, M.D. Philadelphia: Lea & Febiger.

THIS small brochure deals with military surgery, trachoma and acute conjunctival infections and the best methods for the detection of malingerers.

Greenwood has spent some time in base hospital work back of the Allied lines. He is the author of the chapter on surgery. He emphasizes the importance of skilled ophthalmic examinations and points out the ease of overlooking important ocular lesions in the presence of other devastating bodily injuries.

Two interesting measures advocated are the more general use of glass balls or other material implanted following enucleation and some form of suction apparatus in traumatic cataract.

In 4 out of 5 cases of orbital cellulitis Carrell's tubes proved efficient.

The chapter on trachoma and conjunctivitis by de Schweinitz is in that author's characteristic and authoritative style.

Of great value to the draft board examiner is the last chapter on malingerers and their detection.

This brief work should be carefully studied by all men whose medical duties will summon them to cantonments or back of the fighting lines. B. F. B.

AMERICAN ADDRESSES ON WAR SURGERY. By SIR BERKELEY MOYNIHAN, C.B., Temporary Colonel, A. M. S., Consulting Surgeon, Northern Command. Pp. 143; Philadelphia and London: W. B. Saunders Company.

THESE addresses or papers were read in Chicago or elsewhere during the author's recent visit to this country. The subjects are as follows: The causes of the war; gunshot wounds and their treatment; wounds of the knee-joint; injuries to the peripheral nerves and their treatment; gunshot wounds of the lung and pleura. It

was the reviewer's privilege to hear the author deliver the first address, which was a very impressive occasion. All the subjects are handled in the same clear, direct and forcible style. None can be more important to the war surgeon than gunshot wounds and their treatment. In this paper we have a master surgeon, after abundant war experience, laying before us briefly and clearly the various new methods of treatment which have gained recognition during the war and his judgment as to their relative values. In like manner we are treated to a most instructive digest of the work done and the important results obtained in connection with the other conditions discussed. How interesting it is to learn, after all our fears concerning and our efforts to prevent collapse of the lung when the chest is opened, that the thorax is being opened widely, the collapsed lung being delivered, the wounds in it being sewed up as in other tissues, the repaired lung being replaced in the chest and the thoracic opening tightly closed, with a wonderful improvement in the results over those of previous methods of treatment. T. T. T.

PUBLICATIONS OF THE RED CROSS INSTITUTE FOR CRIPPLED AND DISABLED MEN. A BIBLIOGRAPHY OF THE WAR CRIPPLE. Edited by DOUGLAS C. MCMURTRIE.

THIS recently published and up-to-date *Bibliography of the War Cripple* is of timely interest and should prove of great value to students of the subject and to the increasing number of workers in this important field. There is comprised in it a list of references to literature pertaining to the reëducation, employment and other forms of care of crippled soldiers and sailors. The compiler of this bibliography takes pains to make clear that whereas every effort has been made to make it as full as possible within the particular field covered, there have been purposely excluded articles dealing solely with medical or surgical subjects, with the pension system and with provision for the blind, the deaf and the nervously deranged. While the importance of these subjects is recognized, it is felt that they fall outside of the limited scope of this index.

It is stated that practically every entry has been made from the original publications. It is further stated that nearly all the indexed literature is reproduced in either the priyate library of the compiler or the collection of the Red Cross Institute. Both of these collections can be consulted at the library of the Red Cross Institute for Crippled and Disabled Men, 311 Fifth Avenue, New York City. A survey of the titles included in the present publication indicates that most of them are from Continental sources, French and German equally, the balance being made up of English and a few Italian contributions. Provision will be made for current accessions of material along these lines by issuing supplements to the present list. R. P.

FUTURE OF THE DISABLED SOLDIER. By C. W. HUTT, M.A., M.D., D.P.H., Oxford Deputy Medical Officer of Health, County Borough of Brighton; Recently Member of Brighton War Pensions Committee. New York: William Wood & Co.

THIS excellent little book of but 200 pages gives a fund of information regarding the experiences of Great Britain, France and Germany in the matter of reëducating the partially disabled soldier and training him to be an independent member of society. Our problem in this country is going to be very soon brought to our notice and it will do well for all industrial physicians and managers of employment departments of our large industries to study carefully the pages of this book.

The first chapter deals with the arrangements for treatment; then follows chapters on the training of the disabled in the several countries and lastly a chapter on the employment of the disabled.

The opinion seems to prevail that many lines of training should be carried out in trade schools, taking groups of disabled men, rather than encouraging employment in ordinary workshops where the disabled would have to compare himself with able workmen with resulting discouragement. It is also pointed out that the earlier the attempt to induce men to take up training the better, and that whenever possible disabled men undergoing training should be used to convert others.

The general experience is that the men do not avail themselves to the extent that they should of the opportunities placed at their disposal for learning skilled trades. The causes of this disinclination are discussed and remedies suggested.

At the end there is a useful appendix tabulating occupations suitable for defectives. C. N. S.

THE SURGICAL OPERATIONS ON PRESIDENT CLEVELAND IN 1893. By MAJOR W. W. KEEN, M.R.C., Emeritus Professor of Surgery, Jefferson Medical College. Pp. 52. Philadelphia: George W. Jacobs & Co.

IT is fortunate that even at this late date such important historical events as are related in this small volume are now placed on record by one of the principal persons concerned in them. That events of such importance to the public could have escaped the press is marvelous. They are now recorded here and fortified by the notes of those men most responsible in the performance of the operations.

T. T. T.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO T. E UNIVERSITY HOSPITAL.

Carcinoma of the Splenic Flexure of the Colon.—HARTWELL (*Ann. Surg.*, 1917, lxvi) presents a report of 6 cases and a study of the literature. He says that the splenic flexure of the colon is the third most common site for colonic cancer. This growth tends to the production of obstruction, with indeterminate premonitory symptoms. This complication occurs acutely in nearly three-fourths of the cases coming to operation. A recognition of the foregoing facts and a more careful detailed study, with a possible exploratory operation, should lead to an early diagnosis in a majority of the cases and thus forestall acute complications. The probable operative mortality of all cases up to the present time is over 60 per cent., and the percentage of the prolonged cures is exceedingly low, 10 per cent. to 25 per cent. These appalling results are largely due to the delayed diagnosis, and an improper mode of attack. The latter should follow the principle of the two or more stage operation, with provision for external colonic drainage, either as a preliminary, or at the time of resection; always the former in the presence of serious obstruction or abscess formation. The distal portion of the transverse colon, the flexure, and the entire descending colon must be resected in order to obtain the requisite conditions for a secure anastomosis with an ultimate patency of the colonic lumen. Notwithstanding the meager success thus far obtained, attention to the lessons learned from the successes and failures of those who have worked in this field justifies the hope that this lesion may be as satisfactorily dealt with as cancer in other parts of the body.

Pituitary Gland and Generative Organs.—GOETSCH (*Surg., Gynec. and Obst.*, 1917, xxv, 229) says there is a close interrelationship in function between the pituitary and sex glands, a fact supported by abundant experimental evidence and by numerous observations on pituitary disturbances in the human subject. Overfunction of the pituitary anterior lobe is associated with overactivity of the sex glands. Deficiency of pituitary secretion in the individual is followed by under-

development and genital aplasia in the young and by sexual inactivity and retrogression in the adult. Primary alterations of function of the sex glands, as in pregnancy and after castration, are followed by pituitary hyperplasia and hypertrophy. The specific action of posterior lobe extract ("pituitrin," "pituitary liquid") upon the smooth musculature of the uterus and bowel has led to the wide usage of this drug in obstetrical practice and in the treatment of intestinal paresis following abdominal operations. The administration of pituitary extracts is of distinct benefit in clinical states of pituitary underfunction.

The Physiological and Pathological Importance of the Parathyroid Gland from the Experimental Aspect.—VOEGTLIN (*Surg., Gynec. and Obstet.*, 1917, xxv, 244) says that the parathyroid gland has a definite physiological function which is still incompletely understood. The presence of a minimum of parathyroid tissue in the body is essential for life and the continuation of normal metabolism. Parathyroid insufficiency seems to be characterized by an increased irritability of the nervous system to the galvanic current, which may be due to the withdrawal of soluble calcium salts from the blood and tissues. Parathyroid insufficiency leads to an alkalosis which is converted into an acidosis as a result of active tetany. Definite metabolic changes take place in animals after complete parathyroidectomy. Pregnancy puts an extra strain on the functions of the parathyroid, as evidenced by the appearance of tetany during this period in partially thyroidectomized animals. Tetany has been observed during lactation in animals with parathyroid insufficiency. Interruption of lactation was followed by recovery. The offspring of partially parathyroidectomized animals exhibit a marked increase in nerve irritability. An intravenous injection of soluble calcium or strontium salts or hydrochloric acid almost instantly removes the symptoms of tetany. However, tetany may reappear after this treatment and the life of such animals cannot be saved by the continued administration of calcium. The injection of parathyroid extract seems to have a temporary curative effect on tetany animals. Isotransplantation of parathyroids into animals with parathyroid insufficiency is usually successful. The spontaneous recovery from tetany is experimental animals is probably due to changes in their metabolism (acidosis) caused by the hyperactivity of the skeletal muscles during tetany. The experimental facts do not support the theory that eclampsia is due to hypoparathyroidism. A condition which might justly be termed hyperparathyroidism is known at the present time.

The Pineal Gland.—MCCORD (*Surg., Gynec. and Obst.*, 1917, xxv, 250) says that a clinical syndrome is to be associated with disturbances of the functions of the pineal gland. Because of the involution of the pineal at puberty, the constitutional manifestations of pineal pathology appear to be confined to prepuberal years. The essential characteristics (apart from pressure and neighborhood manifestations) are (*a*) early sexual development evidenced in the enlarged genitalia, pubic hair, general body hair, early change in voice; (*b*) precocious mental development, manifested in maturity of thought and speech; (*c*) general overgrowth of body to the extent that a child of six or seven years may

have the appearance of a child near puberty. The experimental extirpation of the pineal gland is surgically possible. The gland is not essential for the maintenance of life. The early symptoms following pinealectomy are attributable to the severe brain injury. No changes attend the removal of the gland in adult animals. As to the effect of pinealectomy in young animals, Sarteschi, Foa and Horrax respectively state that the removal of the gland leads to precocity of development. Exner and Boese and Dandy report no change after pinealectomy. The administration of pineal substance to young mammals is reported to hasten growth and sexual maturity. In unicellular organisms (paramecia) pineal extracts increase the rate of reproduction to more than double that of controls. In larval forms (ranidæ) both growth and differentiation are hastened as a result of pineal feeding. The inference is allowable that the pineal gland is an organ of internal secretion whose functions, however, are of minor significance in the general activities of the endocrinous system.

The Endocrine Function of the Pancreas and its Relation to the Sex Life of Women.—CARLSON (*Surg., Gynec. and Obst.*, 1917, xxv, 283) says that all evidence supports the view that some substance or hormone secreted by the islands of Langerhans into the blood is necessary for utilization of sugar by the tissues. This function is specific for the pancreas. Other endocrine organs may influence sugar metabolism in a superficial way by altering the sugar mobilization (adrenals, thyroid) or by increasing or decreasing the rate of oxidation in the body general. The rest of the endocrine glands cannot maintain the power of the tissues to oxidize sugar in the absence of the pancreas, and the hypoactivity or hyperactivity of other endocrine glands do not produce actual diabetes in the presence of a normal pancreas. While the failure of the tissues to use sugar in the absence of the pancreas is the central and definitely established fact, there are probably other primary defects in the development of acidosis, lipemia, increased metabolism, lowered resistance to infection, etc. All the evidence points to the view that true diabetes mellitus in man is primarily the result of pancreatic deficiency (islets). There is, at present, no evidence of any specific relations of the endocrine functions of the pancreas to the gonads, male or fenale, or to menstruation, pregnancy, and lactation. Absolute diabetes induced after conception leads to death of the fetus. Absolute diabetes probably renders conception impossible. Partial diabetes under careful dietary control permits of normal sex life of women (menstruation, normal pregnancy, normal child, lactation), and pregnancy under such conditions does not aggravate the diabetes. But in the absence of such dietary control the pregnancy aggravates the diabetes in the mother, and uncontrolled diabetes in the mother is extremely injurious to the fetus. There is some evidence that in the late stages of pregnancy the fetal pancreas may function for the mother.

The Surgery of Bronchiectasis.—ROBINSON (*Surg., Gynec. and Obst.*, 1917, xxiv, 194) reports five complete resections of the lower lobe of the lung, with one death. Bronchiectasis is a chronic loathsome disease—generally regarded as incurable. The expectoration is disgustingly

profuse; consequently the afflicted loses employment, shuns society, becomes a recluse and not infrequently resorts to dissipation. He is pale and a trifle cyanotic. His fingers and toes are clubbed. He labors with early fatigue. He coughs spasmodically with varying persistency. Stooping, laughing, eating, hurrying, flood his trachea with pus and he retires, embarrassed, to drain himself of abundant sputum. In winter he is periodically ill with severe "colds" sometimes with bronchopneumonia, nor does the mildness of summer rid him of chronic cough. He may live many years until cerebral abscess, pneumonia, septicemia, amyloid disease, or hemorrhage happily ends his existence. Advanced bronchiectasis cannot be cured by medication, inhalations, intratracheal injections, intratracheal irrigations, climatotherapy or vaccines. Collapse therapy produced either by nitrogen, artificial pneumothorax or by surgical measures is not curative. Pulmonary arterial ligation is of more definite value as a preparation for lobectomy than as a curative measure *per se*. Excision of the diseased portion of one lung is the only curative treatment of advanced bronchiectasis. In the present status of the development of thoracic surgery, lung resections should be performed in two stages or three stages. The several-stage operation of the rib-resection type has been attended in the writer's experience with a 20 per cent. mortality. The operation of intercostal lobectomy has distinct technical advantages. When performed in one stage, an undue risk of life is incurred. The physiological advantages of the several-stage technic may yet be successfully combined with the technical advantages of the intercostal exposure.

THERAPEUTICS

UNDER THE CHARGE OF

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Nephritis from the Stand-point of Urea Excretion.—McLean (*Jour. Am. Med. Assn.*, 1917, lxix, 437) attempts to make clear what actually happens in the condition of urea retention. Urea retention in the sense in which the term is now generally used is not a continuous process of piling up of urea in the blood, due to inability of the kidneys to excrete the large amounts of urea formed in the body, but is applied to any condition associated with an abnormally high concentration of urea in the blood and is taken to indicate disturbed renal function. The kidneys may be able to excrete far greater amounts of urea than they are ordinarily called on to do, even in severe cases of nephritis, while the condition known as urea retention exists in these cases at the lower levels of protein metabolism just as it does at the higher, even though in the former instance the blood urea figure may be within normal limits. McLean reviews briefly the classic work of Widal and Javal

and of Ambard and Weil, and then proceeds to report his own findings in 2 patients suffering from chronic nephritis. Both patients bore the strict dietary regimen well and showed no change in general condition at the end of the experiment, and are still alive a year after the conclusion of the investigation. Because of the length of the experiment the diet was varied more than is usual in metabolism experiments, but analysis was made of all protein-containing food. The intake of fluid and of chloride was kept constant. Twenty-four-hour specimens of stool and urine were analyzed daily for nitrogen. Blood-urea determination and a simultaneous urine analysis on a timed specimen were made twice a week to compute the index of urea excretion. Both cases are exactly similar and show the essential features described by Widal and Javal in their case; that is, a close parallelism between nitrogen intake, concentration of urea in the blood and nitrogen output. A change in nitrogen intake was always quickly followed by a change in the concentration of urea in the blood and in nitrogen output, so that nitrogen balance was reëstablished on a new level. Variations in the diet increased the urea concentration of the blood from 0.262 gram per liter to 2.542. This latter figure is far above the level at which Hewlett, Gilbert and Wickett believe that toxic effects of urea appear, yet McLean's patient showed no uremic symptoms. The findings regarding urea excretion are of special interest: In Case I, with a variation in blood urea from 0.211 gram per liter to 0.855, the index of urea excretion remained remarkably constant, with an average of 21.4. In Case II there is a greater range of variation, the most significant being present when the blood urea reached 2.542 grams per liter. On that day the urea index was 8.3 instead of about 20. This would seem to indicate that here the maximum capacity of the kidney to excrete urea had been exceeded and actual accumulation had begun. This occurred only when the nitrogen intake had been maintained at over 36 grams per day for two days. The 2 cases confirm the findings of Widal and Javal and add the fact that no essential variation in the ability of the concentration of urea in the blood at various levels of protein metabolism was demonstrable until a very high level was reached; that is, the quantitative relationship that existed between the concentration of urea in the blood and the rate of its excretion remained the same at all levels of protein metabolism. McLean believes that he has demonstrated that a relatively increased concentration of urea in the blood follows the increased resistance with which diseased kidneys oppose the passage of urea. When as the result of feeding an increased amount of nitrogen the concentration of urea in the blood rises a parallel increase in the rate of excretion of urea occurs. When a point is reached at which the rate of urea excretion is kept equal to the rate of formation by the organism the level of urea in the blood ceases to rise and the organism remains in nitrogen equilibrium. But when the nitrogen intake is diminished, urea is excreted for a time more rapidly than it is formed, until the level of blood urea falls and reaches a point such that the rate of urea excretion is again equal to the rate of urea formation and the organism is once more in N equilibrium. This is the explanation offered by McLean for the events occurring in the so-called retention of urea.

OBSTETRICS

UNDER THE CHARGE OF

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A Comparison of the Principal Methods in Use at Present for Performing Cesarean Section.—FERRONI (*Annali di Obstetricia*, No. 9, 1916) compares the principal methods now in use of performing Cesarean section. He traces the development of the transperitoneal method and draws his conclusions from a series of fifty-seven sections performed by different methods. These operations were done for contracted pelvis and where the mother was uninfected at the time of operation, good results were obtained. He believes that in the average case, the simple classic method is best, and in performing transperitoneal operation he uses the anterior incision only.

A Comparison of Induced Labor with Delivery by Cesarean Section.—HOFMEIER (*München. med. Wchnschr.*, August 11, 1916) compares the results of these two operations for eight years in his clinic at Wurzburg. In this time there were 76 cases of premature labor and 73 Cesarean sections. In the total 149 cases there was one maternal death, a woman who had been subjected to manipulation and infected before admission to the clinic. The Cesarean operations were suprasymphysial and transperitoneal. The fetal mortality was the same after both operations. The Cesarean patients were convalescent in fifteen days on the average. Where the patient can be procured for operation before the membranes are ruptured the results of Cesarean operation are fully as good for the mother as those of induced labor, and hence the operation as a rule should be preferred.

Pain Over the Uterus.—BEACH (*Am. Jour. Obst.*, August, 1916) describes the case of a woman in her second pregnancy, who had considerable pain over the uterus, and one week before term the patient noticed excessive movement on the part of the child. These were so violent as to prevent sleep. The movements soon became very much less violent and fetal life was still present. When labor began the signs of fetal life ceased with the first pain. The child was finally stillborn spontaneously, with eight coils of cord about the neck. The reviewer recalls the case of a multipara near term who slipped and fell upon a rug which slid from her feet on a highly polished floor. The mother was not much injured, as she struck upon the back. The fall produced little effect upon the mother, but she noticed that fetal movements became excessively violent and then became normal or less than normal. Labor developed and it was necessary to deliver by forceps. The cord was found coiled several times about the neck of the child. The child was asphyxiated and was revived with difficulty, but died of inspiration pneumonia. It seemed fair to believe that the fall had produced violent fetal movements in which the cord became coiled

about the body of the child and the traction upon the cord at birth interfered with the child's circulation and produced involuntary movements of respiration. Through these, material from the genital tract of the mother was drawn into the lungs and set up pneumonia. The reviewer had at one time under his care a primipara, with ample pelvis and fetus of moderate size, who failed to come into labor at the proper time. There was no attempt at engagement or descent. The patient was delivered by elective section and the umbilical cord was found twice around the neck, over each shoulder, and under each axilla. Spontaneous labor was impossible without separating the placenta, which would have immediately caused the death of the child, and threatened the mother with the dangers of concealed accidental hemorrhage. The life of the child was undoubtedly saved by the operation.

Brachial Birth Palsy.—THOMAS (*Am. Jour. Obst.*, April, 1916) contributes a paper upon this subject and gives a summary of 11 cases. The paper is well illustrated by photographs. In cases in which there is no displacement of the shoulder-joint a perfect recovery will be obtained from exercise alone. The condition is considered of great importance, and is believed to be the result of trauma occurring during birth. As soon as possible, if there is dislocation, a complete reduction should be attempted, and whether reduction is complete or not, vigorous and prolonged exercise afterward will improve the motion in the joint. Reduction by non-operative methods calls for the application of such great force that it is exceedingly dangerous. In operation the joint is freely exposed, the deltoid divided from the upper end of the humerus, and the obstructing portion of the acromion is removed. This is usually cartilaginous and can be cut with a knife. Efforts should then be made to bring the arm to external rotation and abduction and the head of the humerus as nearly as possible in its normal position. It will often be impossible to accomplish complete reduction because of the traction of tendons and their tissues, but almost always considerable improvement can be obtained. It may be necessary to divide the insertion of the subscapularis before external rotation can be obtained. The wound is closed with continuous plain catgut sutures and a sterile gauze dressing applied with a light plaster cast.

Pyloric Obstruction in Infants Treated by Operation.—DOWNES (*Surg., Gynec. and Obst.*, March, 1916) publishes a paper upon this subject in which he gives a summary of his experience in 66 cases observed in five and one-half years. With one exception there was the characteristic tumor at the pylorus, consisting of marked hypertrophy of the band of muscle fibers with thickened mucous membrane lying in longitudinal folds. In the one exception noted the baby died, and on autopsy a small tumor originating in the muscular mucous tissue was filling the lumen of the pylorus. Most of the stomachs were of average size, one so small that it would hold but one ounce. There was edema in varying degrees in all. The symptoms are projectile vomiting, tumor, peristaltic waves, gastric retention, and rapid loss of weight. Marked constipation is usually present, and a tumor can frequently be felt. In a previous series of 61 cases the mortality was 22 per cent. These were treated by gastro-enterostomy. This has been abandoned, and

Rammstedt's method has been given a thorough trial. In 19 done after this method a sound was passed through the pylorus after the muscle had been divided. The operation consisted in incising the tissues of the pylorus longitudinally down to the mucous membrane but not through it. The tissues are then stretched gently by the finger. Of partial pyloroplasties there were 8 deaths, a mortality of 23 per cent. The postoperative treatment consists in very careful and limited feeding, and usually something is given the child in about two hours after the operation. From 2 to 3 drams of breast milk, alternating with water, is selected. This is gradually increased until the child comes up to the normal standard. In favor of the operation is the fact that it is simple and that it permanently removes the obstacle.

Enlarged Thymus in Infants.—HERRICK (*Surg., Gynec. and Obst.*, March, 1916) describes 6 cases of enlarged thymus in infants, and calls attention to the difficulty in diagnosis between enlarged thymus and great enlargement of the mediastinal glands. In enlarged thymus the dulness is higher up with a notch between it and the heart area, whereas when dulness comes from enlarged glands it is near the bifurcation of the trachea and vessels. Examination by the *x*-rays will often assist. A thymus case is usually well nourished, but pale and pasty, with no tubercular history. A tubercular case may be reduced in flesh, less vigorous in appearance, and have slight elevation in temperature. As regards treatment, operation is dangerous and uncertain, and probably the *x*-ray is the most satisfactory method. Of the 6 cases, 3 recovered and 3 died. The *x*-ray treatment seemed successful and is the only treatment which could be safely employed in such frail patients.

Obscure Fever in the Newborn.—COPELAND (*Jour. Am. Med. Assn.*, November 4, 1916) finds that the nervous instability of infants is frequently a cause for considerable rise in temperature which may continue over varying periods. Such infants are apt to be rachitic and frequently show evidences of tetany, laryngismus, stridulus, and general convulsive seizures. Obscure inflammation of the middle ear is another cause for the development of fever. Obscure disease of the tonsils, even in very young children, may also be a cause. The paper emphasizes the necessity for careful examination in these cases.

Influence of Syphilis on the Production of Children.—HARMAN (*British Med. Jour.*, February 5, 1916) in studying 1100 children to ascertain the percentage of blindness, found 150 family histories in which syphilis appeared as a cause of congenital or inherited disease. In 68.5 per cent. of the blind children the Hutchinsonian teeth were present, and there were other symptoms in addition. In direct contrast with these are the histories of 150 families where it was known that syphilis was not present. The 150 syphilitic mothers had 1001 pregnancies, but of these only 390 resulted in the birth of fairly healthy children. On the other hand, the 150 healthy mothers had 826 pregnancies, and from these there resulted 654 healthy children. It is interesting to observe that the syphilitic mothers had 17 per cent. more pregnancies than the healthy mothers. This may be accounted for, at least in part, by the frequency of miscarriages and stillbirths in a syphilitic, and the

short interval between many of these would allow of several ineffective pregnancies in the same time that would be taken for one full-term pregnancy in a healthy mother. The results of these comparisons are sufficiently striking to indicate the great importance of syphilis in diminishing fertility.

Spontaneous Evolution during Labor in Shoulder Presentation.—CARTER (*Surg., Gynec. and Obst.*, November, 1916) describes the case of a multipara whose previous labors had been successful, but in the one described had prolapse of an arm followed by cessation of active uterine contractions. On examination the left arm was prolapsed, the scapula anterior, and the arm was of good color. The cervix was fully dilated and the shoulder was firmly wedged into the pelvis. It was impossible, without using more force than was prudent, to carry the hand upward into the uterus to perform version. As the patient was not having hard pains and her general condition was good she was taken to the hospital in a motor car. This seemed to do her no special harm. A few moments after entering the hospital the pains increased in number and intensity, followed by violent bearing-down efforts at intervals of two or three minutes. She was immediately given a light anesthetic and placed upon the operating table. The prolapsed arm had now become very much swollen and congested and the shoulder had rotated beneath the pubis. The chest, abdomen, and breech were consecutively forced over the perineum. The head was extracted without difficulty and the placenta followed within five minutes. The child was dead, but death had evidently been very recent. The reviewer recalls the papers of the late Dr. King, of Washington, in which he described spontaneous evolution in shoulder presentation, transverse position, and recommends the squatting posture for the patient. In this the thigh of the mother nearest the fetal head was to be considerably advanced, and it was thought that by this maneuvre additional pressure was brought to bear upon the fetal head to force it upward so that the breech might come into the pelvis. He described several cases in which spontaneous evolution was successful. In the observation of the reviewer he was called on one occasion to a woman in active labor, finding a shoulder presentation, transverse position, and sent immediately for assistants for etherization. Before they arrived following two especially vigorous uterine contractions spontaneous evolution occurred and the child was expelled in breech presentation. In this instance the mother insisted upon squatting upon the floor by the side of her bed, inclining the trunk of the body forward and resting the weight of the head and shoulders upon the bed.

Migrating Phlebitis.—HEDBLOM (*Jour. Am. Med. Assn.*, 1916, lxvi, 1777) reports the case of a woman, aged twenty-eight years, in her fourth pregnancy occurring during five years. The first two children had died of exhaustion, the third was living and well. At the end of twelve hours a fairly developed child was spontaneously born. There was no laceration and the placenta came away spontaneously. The uterus did not contract well and there was more than the usual loss of blood. On the eleventh day of the puerperal period the patient had severe night-sweat followed by fever. The white blood corpuscles were

17,000; hemoglobin, 60 per cent. There was inflammation of the right saphenous vein which gradually subsided. This was followed by inflammation of the other veins in the left side of the neck, axilla, arm and chest. This subsided, to be succeeded by swelling in the other portions of the body. In all the patient had six relapses, each attended by more or less severe constitutional prostration. The patient finally recovered and was discharged in the nineteenth week in good general condition.

OTOLOGY

UNDER THE CHARGE OF

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Prevalence of Ear Injuries and Diseases in the French Army.—BRYANT (*Jour. Laryngol., Rhinol. and Otol.*, vol. xxxii, No. 11). The importance of the inclusion of provision for the care of the war deaf in the United States is emphasized by the author. In his record of observations in the French service the number of cases of ear injuries and deafness exceeded those of other observers in the English or Italian services, the ear cases being nearly as numerous as the eye patients, although there have been more cases of total loss of function among the eye cases than among the ear cases, with correspondingly more rapid recoveries, and a larger proportion of cases of very considerable impairment of hearing than of sight, the proportion of ear cases to the total number of cases in the evacuation hospitals being 16 per cent., about 80 per cent. of all ear cases showing considerable impairment of function. The nature of the injuries and their complications are included in three categories: rupture of the sound-transmitting apparatus of the middle ear and its complications; suppuration, acute and chronic; mastoiditis; mastoid abscess and its sequence; injuries of the terminal nerve-ending apparatus, of which the cochlear branch is always the more vulnerable, these injuries being of sudden occurrence or gradual implication and due severally to the larger use of high explosives and the more continued effect of powerful detonation than has ever been previously experienced. As the result of the explosion of powerful shell mines, hand grenades, bombs and rifle explosives causing, in addition to rupture of the membrana tympani, hemorrhage, ecchymoses, and, luckily, limited disintegration of the sound-transmitting apparatus, there is, in consequence of long exposure to loud noise, interference with the nutrition and causation of microscopic changes in the terminal end apparatus, a progressive impairment of hearing, grave in its extent and more or less permanent in its degree. Soldiers entering the war with an auditory apparatus intact are more liable to escape injury than those who have been the subject of previous inflammatory process of the middle ear or some measure of impairment or morbidity of the sound-transmitting apparatus. In addition all forms of dry otitis are subject

to a rapid increase in their tissue change under exposure to excessive irritation of loud sounds, the clinical histories of many of the ear patients showing the rapid sequence of degenerative, dry inflammatory conditions of the middle ear following ear injuries at the front. Ruptured tympanic membranes heal without suppuration, and with restoration of function in from five to twenty-one days under proper aseptic treatment, the duration of the impairment being much prolonged by the occurrence of suppuration, the convalescence being considerably shorter than in cases of middle-ear suppuration in civil practice, uncomplicated middle-ear suppuration yielding quickly to dry treatment, probably because the condition is primarily traumatic and not due to some underlying systemic condition. The treatment of rupture of the drum-head and the prevention of complications is effected by the encouragement of spontaneous repair, secured by the prevention of infection, the treatment being aseptic dry treatment, removal of the moisture in the meatus by wiping, insufflation of sterile boric acid powder and plugging of the external canal with sterile absorbent cotton painted with collodion, this treatment being repeated sufficiently often to secure the desired protection against a suppurative process, the treatment of suppurating middle ears and consequent complications being the same as that required in civil practice. In lesions of the auditory nerve the acute cases give the best prognosis, but complete restoration of function cannot be expected, the treatment of these cases being prolonged rest, with general hygienic attention. In cases of nerve lesions of gradual onset, as the result of continued exposure to loud noises, no improvement was to be expected.

Apparatus for the Application of Cold Air to the External Canal.—GRANT (*L'Organe de l'Audition*, Juin et Aout, 1916). In view of the number of cases with sequence of acute or suppurative middle-ear disease examined for military service, the caloric test, by means of the injection of cold and warm water into the external auditory canal, is open to the objection of the possibility of reawakening the activity of a past inflammatory process, and less injury is likely to result by the application of either the galvanic test or, for purpose of control, a dry caloric process, for which purpose the author's instrument serves an excellent means of application. This instrument consists of a tube of metal, of good conductivity copper for instance, in the form of a spiral, with a removable tip to the end of the tube to be inserted into the external auditory canal, permitting removal and sterilization. The cone of tubing is covered with an absorbent gauze saturated with ethyl chloride, the evaporation of which chills the tube and, correspondingly, the air which is passed through it by means of a thermos cautery bulb, the desired degree of chill being attained in from ten to fifteen seconds after the saturation of the gauze. This instrument was first described as a cold-air labyrinth test apparatus in the *Lancet*, in July, 1914, and has achieved value in subsequent tests incident to war conditions.

Changing Methods and Advances in the Treatment of Progressive Deafness from Chronic Secretory Otitis Media.—EMERSON (*American Laryngological, Rhinological and Otological Society, reported in Laryngoscope*, January, 1918). In this paper the author desires to draw atten-

tion to the importance of the consideration of possible remote causes of infection operating systemically to actuate progressive changes in the middle-ear sound-transmitting apparatus in distinction from those more immediate exciting causes in the nose and nasal pharynx, basing his communication upon the results of a questionnaire as to the expectation of improvement in such cases from treatment of the nasopharynx, excluding the epipharynx and inflation of the middle ear. To prove that positive improvement in hearing resulted from the cure of remote foci was not an easy problem, as the testimony of the patient, or the aurist, was of no scientific value unless such observations were supported by careful hearing tests, and records covering a term of years, for one was dealing with a chronic disease, subject to acute exacerbations, and varying acuity of hearing. Further, in order that such records should be available for analysis, such observations should extend over a period of from three to five years. From his study of the subject the following conclusions were drawn: "(1) Every case of chronic progressive middle-ear deafness has a primary focus; (2) such primary focus is usually constant for the individual; (3) every case showing variable hearing can usually be improved up to their best hearing; (4) Inflation in chronic cases is unscientific and harmful as a routine; (5) nasal obstructions do no harm to the middle ear unless infection is present; (6) foci wherever found are potential factors in the progress of chronic progressive otitis media; (7) no hearing test will forecast the improvement in a given case as long as we have a positive Rinné with variable hearing; (8) whatever the microscopic appearance of the membrana tympani, the cause of the deafness is active for a long time outside the middle ear as a toxemia or low-grade infection subject to acute exacerbations."

Acute Suppurating Mastoiditis without Tympanitis: Perisinus Abscess, Phlebitis, Streptococcemia, Operation, Recovery.—Long says (*Ann. Otol., Rhinol. and Laryngol.*, June, 1917) that the case here reported by the author illustrates the possibility of extensive infection of the mastoid, with considerable destruction and serious complications, with only a minimum degree of evidence of disturbance in the tympanic cavity, which served as a transitional medium between the point of primary infection and its ultimate exhibition. A girl, aged twelve years, with the history of severe pain in the left ear of five days' duration, accompanied by chills, fever, nausea and vomiting, sleeplessness and delirium, with severe pain and tenderness in the left mastoid region. Temperature, 104.2; pulse, 120; respirations, 36, but without discharge from the external auditory canal, no apparent inflammatory process within the tympanic cavity, and with a membrana tympani moderately reddened, and with the larger bloodvessels injected. An incision of the drum-head liberated no fluid other than blood, and the gauze inserted in the auditory canal and removed the following day was marked only by the dry blood from the incision which had in no way tended to an abatement of the symptoms, except that there was less complaint of pain in the head; the patient was more toxemic, sleepless and delirious. On the ninth day symptoms of meningitis were still more pronounced and the simple mastoid operation was determined upon. The inner table was found carionecrotic, the greater portion being removed by

the curette, exposing small pockets of pus and masses of exudate which completely covered the sinus, and the bone was removed in every direction until healthy dura appeared. The examination of the vein from the knee to the tip of the jugular bulb gave no evidence of thrombus and a long incision gave a free hemorrhage from both ends without clots. This hemorrhage was controlled by packing, with a superposition of moist dressing. On the day following the operation there was no marked improvement, but the tongue was moist, but meningeal irritation had not increased. The laboratory finding of pus from the mastoid showed streptococci. On the next day, there being little change in the condition, a lumbar puncture was made. The spinal fluid was found normal and not under pressure. Under these conditions the treatment consisted in nursing, the necessary surgical dressings, and the patient made a good recovery, being able to leave the hospital twenty-three days after the operation.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Observations on the Stability of the Erythrocytes of the Ox, Pig and Sheep.—Though it is customary to use sheep's corpuscles in preparing the usual amboceptor for the Wassermann test, experience has shown that these elements in the Noguchi method are not so stable nor so resistant to human sera as the corpuscles of various other animals. LYON (*Jour. Infect. Dis.*, 1918, xxii, 49) showed that erythrocytes of the ox and pig give even better results than those of the sheep. A working amboceptor was made after five intravenous injections of ox corpuscles into a rabbit and proved to be so satisfactory with the Noguchi method that the sheep system was gradually abandoned and the ox system used exclusively, employing two antigens, alcoholic extract of human heart and cholesterinized extract. Experiments were made by testing the erythrocytes of the pig as well as those of the sheep and ox with a varying number of human sera, 123 in all. In no instance were the sheep cells more resistant than those of the ox or pig. No satisfactory explanation of this fact can be given. There is no explanation nor proof other than the observed fact that human sera contains a natural antisheep amboceptor. Zoölogically the sheep and the ox are closely related, and one would expect their corpuscles to behave similarly under the influence of a serum obtained from an animal as zoölogically remote as man. On the other hand, the zoölogically unrelated ox or pig behave similarly, so far as their erythrocytes are concerned, under the influence of human serum. The well-known ease with which the antisheep amboceptor can be prepared appears in part at least to depend on some inherent weakness of the sheep erythro-

cytes. But the fact that they are unstable makes their use in complement-fixation tests with human serum unreliable. Ox erythrocytes seem to have better keeping qualities than the erythrocytes of the pig or sheep.

Studies in Immunity against Staphylococcus Pyogenes Aureus.—The important part played by liver and spleen in ridding the blood stream of infecting organisms was emphasized years ago by Wyssokowitsch and Werigo. Recently, BARTLETT and OZAKI contributed a very enlightening paper (*Jour. Med. Research*, 1917, xxxv, 465) on the same subject, showing the relationship of phagocytosis of bacteria by these organs and by the lungs. In continuation of this study, ITO (*Jour. Med. Research*, 1917, xxxvii, 189), of the same laboratory, has considered the fate of living staphylococci when introduced into the jugular vein of actively immunized dogs and of killed bacteria introduced intravenously into normal dogs. Positive agglutination in dilutions of 6000 to 10,000 was used as the index of immunity. The animals were killed at periods varying from ten minutes to ninety-six hours after the last injection. Bacteria could not be found in blood smears later than one hour after injection, and they never reappeared. No mention is made of cultures. In the dog killed ten minutes after injection very few cocci were seen in the blood smears, and these were within the leukocytes. The bacteria had disappeared from the tissues within twenty-four hours. The author's conclusions are as follows. "(1) Bacteria introduced into actively immunized dogs disappear sooner than in normal dogs, and never were found in any part of the body. (2) Bacteria that accumulate in the lungs in the earlier stage are transported to other organs, but they are not found in the spleen in large numbers, while they are more numerous in the liver; (3) in the several organs it appears that both fixed and wandering cells have the ability to engulf, as well as to digest, bacteria throughout all stages; (4) as to the fate of the killed bacteria introduced into normal dogs, they are destroyed somewhat more quickly than the living bacteria introduced into immunized dogs and they provoke no changes evident histologically in the tissues." OZAKI (*Jour. Med. Research*, 1917, xxxvii, 247), in order to study the phagocytic properties of fixed tissue cells, perfused the excised spleen of a dog with Locke's solution for some hours and then injected into the organ a culture of Staphylococcus aureus, not through the blood channels but directly into the pulp. As a control the same organisms were injected deeply into the spleen *in situ* in the living animal. "Wandering cells, as well as fixed tissue cells, show, if at all, but slight necrobiotic changes, and their function is well carried out in so far as bacterial ingestion is concerned." In the spleen of the living animal, as well as that kept alive by means of Locke's solution, the bacteria injected into the parenchyma are principally ingested by splenic cells, polymorphonuclear leukocytes and to some extent also by living endothelial cells and endothelial leukocytes. In the living animal the grade of phagocytosis by the polymorphonuclear leukocytes found in the spleen is on an average far more pronounced than that by splenic cells. A similar relation is also observed, although somewhat less marked, within the spleen tissue kept alive by means of Locke's solution, provided that these cells do not undergo any, even slight, necrobiosis.

A Contribution to the Study of War Nephritis.—Since the beginning of the war a number of papers have appeared dealing with the occurrence of nephritis among soldiers on active duty. The various observers have insisted upon the occurrence of a disease among soldiers which bears no relation to any previous kidney infection or systemic illness as may be found in civil life. It is obvious that with the aggregation of such large numbers of men there will be found sporadic cases of recurrent nephritis which escaped the attention of the recruiting officers. Besides this, with the appearance of active infections like typhoid, dysentery, pneumonia or those of the heart, Bright's disease in different grades of severity are met with in the frequency seen in civil hospitals. Over and above this, however, there has appeared a type of nephritis bearing no relation to a previous illness nor appearing as a complication of another disease. This form of nephritis has occurred among the men on active duty in the trenches, while the soldiers who have not been on the firing line and the civilian population in the near vicinity are relatively or completely immune to the affection. DUNN and MCNEE (*British Med. Jour.*, 1917, ii, 745) have lent particular attention to the study of nephritis and have collected many cases among the British Army at the front. For obvious reasons they are unable to state the exact number of men examined and the incidence of the disease. They point out that they were unable to associate the varying incidence in different companies with the climatic conditions nor with the conditions under which the men were living. The disease may be very insidious in its onset, the most common clinical manifestation being dyspnea. Next in frequency they found edema, pain in head, epigastrium or back, sore throat and hoarseness, in the order named. The edema appeared as a puffiness about the face or extremities. Fever was present in only a few cases and uremia was rarely seen. The urine contained large quantities of albumin, but showed little diminution in quantity. Casts were always present in varying numbers. The bacteriological examination of the urine showed the presence of bacteria in more than half of the cases examined, the streptococci being the commonest organisms found. The authors had an opportunity of studying the tissues from 35 cases of true war nephritis, in which the characteristic lesion was of the glomerular type. The glomeruli were cellular, showing some leukocytes and lymphocytes, but never showing blood thrombi. Granular occlusions of the glomerular loops were observed in a few cases. A true inflammatory exudate was wanting and the interstitial tissue between the tubules showed but little reaction. Various grades of degeneration of the tubular epithelium was observed, but it was never the outstanding change. The medulla of the kidney showed an edema and hyaline change of the connective tissue. The authors also observed peculiar changes in the lung. These consisted of an interstitial edema, without an associated pneumonic process. The lung lesions, they claim, are suggestive of a respiratory irritant, not unlike that obtained in gas poisoning. In the brain, minute hemorrhages about small vessels were also seen. The authors state there is no evidence that the nephritis is due to bacterial infection. They suggested a relation between the pulmonary lesion and the changes occurring in the kidney

Experimental Immunity to Cancer.—Bulloch and Rohdenberg (*Jour. Cancer Research*, 1917, ii, 455 and 465) have contributed some interesting experiments on the relation of induced cancer immunity to tissue growth and tissue regeneration and on the possibilities of an immune influence by splenectomy. Immune substances seem to arise from living cells, whether from the products of metabolism of their growth or of their death or of growth followed by death. The growth power of embryo cartilage is greater than that of embryo skin, yet when the former was injected into one series of rats, and the latter into another, and both series shortly inoculated with Flexner-Jobling carcinoma, the percentage of immunity to this was as 19 to 30, *i. e.*, in favor of those rats injected with embryo skin. The authors suggest that superiority of the skin in cell elements and in active proliferation may account for its greater power for stimulating immunity. To determine the immunizing action of degenerative metabolites, large doses of embryo skin were injected for purposes of immunization and degenerative changes occurring early, much necrotic material resulted. Later these rats were injected with Flexner-Jobling carcinoma, and this material was removed and studied in various stages of degeneration. Fully two-thirds of it showed complete degeneration before the fifth day, but immunity had not arisen in all. "It is impossible to determine by the local reaction of the animal toward the immunizing agent, or by the condition of that agent, whether an animal will be susceptible or immune to a transplantable tumor." These workers then wished to investigate whether increasing absorption of products of cell-degeneration might not favor immunity, and they used the Flexner-Jobling carcinoma, which does not produce concomitant immunity nor that which arises when a tumor grows for a period and then recedes. Degenerative products were obtained by transplanting into the shoulder of a rat the tumor mass which for eighteen days had been in its side. Eleven days later the same tumor strain was injected, but the degree of immunity was about the same in these rats as in the controls. In another experiment it was shown that an initial small dose gives more immunity than a large one. The authors conclude that "induced immunity to transplanted cancer is not solely due to growth or the metabolites of growth of the immunizing agent, nor is it due to death and the degenerative metabolites of the injected material." The experiments involving splenectomy were performed because of the alleged influence of lymphocytes in immunity to transplanted tumors. Using a tumor which is spontaneously absorbed, they showed that "splenectomy does not influence the persistence of immunity in animals." Neither did removal of spleen affect the regression of a previously injected tumor producing concomitant immunity. Removal of the spleen or testes had no effect upon the immunity induced in adult mice by embryo emulsion. Further, splenectomy neither increased the percentage of takes nor favored the growth of spontaneous tumor grafts.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Drinking-water on Interstate Carriers. — COBB, WILLIAMS and SETTON (*Public Health Reports*, October 13, 1916, xxxi, No. 41) state that the frequent occurrence of typhoid fever among sailors on the great lakes first caused investigators to make a study of this problem. In 1913 the interstate quarantine regulations were so amended as to put the control of drinking-water supplies aboard interstate common carriers under the supervision of the U. S. Public Health Service. The regulations which govern the water supplies of interstate common carriers are briefly as follows:

"*Sec.* 13. Water provided by common carriers on cars, vessels or vehicles operated in interstate traffic for the use of passengers shall be furnished under the following conditions: (*a*) Water shall be certified by the interstate sanitary officers or the State or other authorities within whose jurisdiction it is obtained. (*b*) The ice shall be produced under proper conditions if it is to be used in contact with the water. (*c*) Water containers shall be cleansed at least once a week.

"*Sec.* 14. Interstate carriers shall not furnish their crews with contaminated water nor shall they maintain any receptacle, tank or article which may contain impurities which may affect said water.

"*Sec.* 15. No person, firm or corporation shall furnish water for drinking or cooking purposes to any vessel in any harbor of the United States which has been taken from any harbor or place where it may have been contaminated.

"*Sec.* 16. Common carriers shall not furnish for the use of passengers in interstate traffic any water taken from a lake or stream over which the vessel is being navigated unless this water is certified by the U. S. Public Health Service or State or municipal authorities as conforming to the bacteriological standard for drinking-water promulgated by the Secretary of the Treasury."

To carry out these regulations the continental United States was divided into 12 interstate sanitary districts, one of which is the district of the Great Lakes with headquarters and laboratory at Chicago. There are two methods generally used to obtain water on lake vessels, by pumping or by gravity through a sea-cock, consisting of a flanged valve bolted directly to the shell of the vessel in the hull, and secondly, by filling the drinking-water tanks through a hose from a hydrant on shore. These tanks are usually well aft and are constructed of heavy galvanized iron or sheet steel, very few of them being lined. Sometimes

the construction is faulty, permitting contamination from various sources. On most vessels there are two and sometimes three systems of water supply: the drinking-water which supplies drinking fountains, kitchens and wash basins, the "sanitary" system which furnishes the water for flushing toilets, and the fire system which is also used for washing down decks and other purposes. The drinking-water system is the only one under consideration. The water is distributed either by gravity from a storage tank located on an upper deck or by a special distributing pump which maintains a constant pressure in the system. Investigations of these systems of taking in and distributing water have revealed the fact that there are many opportunities for contaminating the drinking-water thus obtained. Among these are contamination of the sea-cock or suction pipe while in polluted water, faulty placing of valves, failure to close the valves, contamination from the sewage system of the ship and accidental or intentional taking of supplies in polluted water. Because of the poor quality of the water obtained, it has been necessary for each vessel to install some form of water purification apparatus. The most common form of treatment is the use of rapid sand filters which this investigation proved to be of extremely low bacterial efficiency. Other vessels used the ultra-violet ray sterilization, eleven of the vessels having the pressure type of apparatus and two the gravity type. The objections to this method were several: the voltage was not high enough to obtain a sufficient intensity of the ultra-violet rays, there was often a sudden fluctuation of voltage, causing the lamps to go out; and the efficiency of the ultra-violet lamps was lowered because the water exposed to the rays was not clear. On five vessels, the water supply was treated with calcium hypochlorite. The efficiency of this depends on the proper proportion being added to the tanks, and this proportioning was not carefully done. Another method of chlorine disinfection was by using an apparatus for treating the water with liquid chlorine. This machine is rather complicated and as the chlorine solution is constantly becoming diluted, it requires chemical tests on the treated water to know just when this solution becomes too weak to be efficient. The apparatus which treated the drinking-water by heating with a steam jet, while it produced good results under careful management, was liable to be mishandled. A total of 961 samples were collected and examined from 74 passenger steamers and 33 freight vessels. The results from these examinations showed that the methods of purification are inefficient, only 38.9 per cent. of the samples treated in rapid sand filters conforming to the standard and only 31 per cent. of the samples treated by the ultra-violet ray method. Of the samples treated by the heat method, 69.2 per cent. conformed, of those disinfected with hypochlorite, 60 per cent. conformed and of those treated with the liquid chlorine, 84.2 per cent. conformed. A study of results according to the route of the vessels showed that those travelling in polluted waters and docking in contaminated harbors showed that the samples from such vessels had a higher bacterial count than from vessels running in better water. In concluding, the authors recommend as the ideal apparatus for water purification, the still. It requires but little care, and it is not necessary to pay attention to the place of taking the supply of water. They have demonstrated that heating by steam jet and exposure to ultra-violet rays are capable of producing a water conform-

ing to the standard if everything about the apparatus is in good order and it is carefully operated, but, as experience has shown that these conditions usually do not exist, purification by means of a still is far more satisfactory.

The Grading of Milk in Small Communities.—WILLIAMS (*Am. Jour. Public Health*, October, 1916, vol. vi, No. 10) states that prior to the enactment of the Sanitary Code in New York State, comparatively few small communities had progressed very much in grading the milk supply. Although it has decided limitations, the grading of a milk supply is by far the most satisfactory method of improving the sanitary quality of the milk supply of a community. For a number of years the 3 first-class cities in the State of New York have kept the milk supply under a satisfactory system of supervision, but in the 7 second-class cities only 1 had any system of grading the milk supply and of the 47 smaller cities of the State, that is, having a population of less than 50,000, only 2 made any definite attempt to grade their milk supply prior to the adoption of the Sanitary Code. The adoption of this code has caused an improvement in the milk supply throughout the State of New York. The articles of this code charge every municipality with the duty of supervising its milk supply through its health officer and his agents. They consist in the inspection and scoring of dairies and the classification of the milk into grades, according to the dairy score and bacteriological count. The tuberculin test and bacteriological count are required for certified and grade A milk and physical examination, excluding tuberculous cattle for grade B milk. Previous to the adoption of the Sanitary Code, the village of Saranac Lake worked out quite an effective system of grading its milk supply, the three grades adopted being very similar to those adopted later by the State Department of Health. The city of Ithaca started in 1909 to improve its milk supply. The milk was graded on the basis of bacteriological counts and on the standard score card. A physical examination of all the dairy cattle supplying milk to the city was required and the dairy scores, giving the bacteriological count and grading for the month were published. In other small communities some provisions have been made for grading the milk supply and an improvement of the scores and bacteriological counts has been noted but this work was limited. However, since the adoption of the State Milk Code many incorporated villages and small cities are now actively carrying on campaigns for grading their milk under the direction of the health officer and an effort is being made to explain to local dealers the meaning of the regulations which require the grading of milk. Thus, at the completion of the first year of work after the adoption of the milk code, a great improvement is shown in the milk supply of small communities throughout the State.

The Prophylactic and Therapeutic Properties of the Antitoxin for Bacillus Welchii.—BULL (*Jour. Exp. Med.*, October, 1917) reports that the results of his experiments with the preventive and therapeutic applications of the antitoxin are highly suggestive. They derive significance from the fact that Bacillus welchii infections in guinea-pigs and other susceptible animals are comparable with infections with this organism in man. The experimental infections in the guinea-pig differ,

however, from the natural infection in man in two important points: (1) man possesses a higher natural resistance to infection; (2) the guinea-pigs were infected with fresh virulent cultures, while man must, in the great majority of instances, derive infection from spores. Moreover, the protected guinea-pigs were given many lethal doses of the living cultures. Such massive inoculations do not occur in man. It may therefore be safely predicted that man will not develop the infection as long as his body fluids and tissues contain adequate qualities of the antitoxin. The possibilities of this passive serum protection has natural limits of time, depending upon the rapidity of elimination of the foreign serum. The experimental data presented by Dr. Bull, which agree with the experience with antidiphtheritic and antitetanic antitoxins, indicate that, in all probability, a passive immunity to Bacillus welchii infection of at least two weeks' duration can be conferred upon man by a single injection of the antitoxin. This immunity will be sufficient in the majority of instances, since only sporadic cases of Bacillus welchii infection arise later than the tenth day after injury, and the greater number occurs within forty-eight hours of that time. In the light of the results obtained by Bull in treating the infection in guinea-pigs, he regards it as reasonable to hope that the antitoxin will be of value also as a therapeutic agent. The indications are that early infectious cases can be readily arrested and the more advanced and severe ones ameliorated, if not wholly checked, so that surgical interference may be resorted to with greater probability of effectiveness. The antitoxin in man should be administered intravenously and probably locally about the wound as well.

A Graphical Study of the Epidemiology of Poliomyelitis. HULL (*Am. Jour. Pub. Health*, October, 1917, vii, No. 10, p. 813) concludes from his studies that poliomyelitis follows the main routes of travel, indicating that it is probably carried by human agencies. It spreads in waves over the country, the crest progressing steadily away from the focus. This suggests that in severe outbreaks practically everyone is exposed, and, after all the susceptibles have been striken, the epidemic subsides. The seasonal prevalence is quite marked, the large majority of cases occurring between the first of June and the last of November. In the southern hemisphere the seasons are reversed, the epidemics occurring between the first of December and the last of May. Out of 34 epidemics occurring during the last seventy-five years, 76 per cent. began in months of deficient rainfall and in 29 per cent. of them the dry weather lasted clear through. Twenty-four per cent. of the epidemics began in excess months, and in none did the wet weather continue clear through. In 18 epidemics with a total of 13,365 cases practically 90 per cent. of the cases occurred during deficiency months. The dryer the weather, in general, the greater has been the number of cases.

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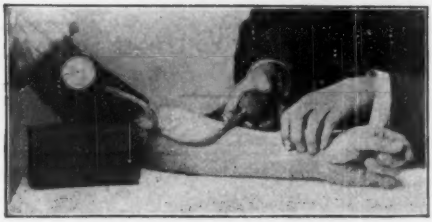

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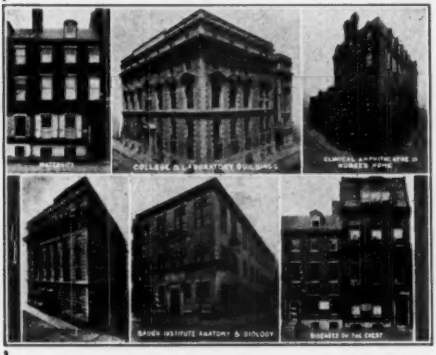

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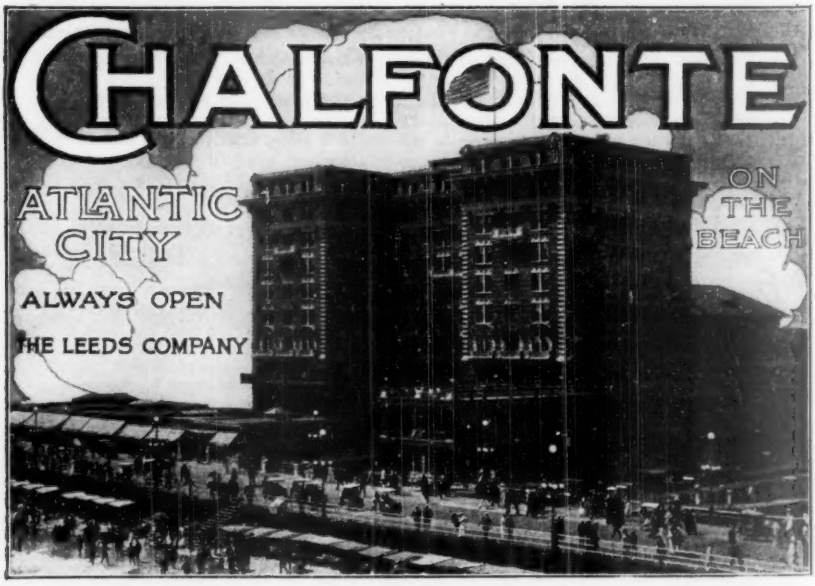

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ARMY MEDICAL CORPS EXAMINATIONS

The Surgeon General of the Army announces that preliminary examinations for the appointment of first lieutenants in the Medical Corps, U. S. Army, are being held at numerous points throughout the United States, on the first Monday of each month.

Full information concerning the examination may be procured upon application to the "Surgeon General, U. S. Army, Washington, D. C." The essential requirements to securing an invitation to report for examination are that the applicant shall be a citizen of the United States, between 22 and 32 years of age, a graduate of a medical school legally authorized to confer the degree of Doctor of Medicine, of good moral character and habits, and shall have had at least one year's post-graduate hospital interneship.

The Government cannot pay to applicants any portion of their expenses incurred in connection with their examination, and due consideration, therefore, will be given to localities from which applications are received, in order to lessen such expenses as much as possible.

Chemistry and Physics have been eliminated as subjects of the examination.

Those applicants who successfully pass the examination are commissioned first lieutenants in the Medical Reserve Corps, and sent to either the Army Medical School in Washington, or to a training camp for a course of instruction, covering a period of approximately three months, during which time they draw the pay and allowances of their grade. If, at the close of their instruction, they pass the final examination, and are favorably recommended, they are commissioned first lieutenants in the Medical Corps of the Regular Army.

The Medical Corps consists of commissioned officers in number approximately equal to seven for every one thousand of the total enlisted strength of the Regular Army authorized from time to time by law, proportionally distributed among the grades and in the ratios as follows: Colonels, 3.16 per cent.; lieutenant colonels, 5.42 per cent.; majors, 23.7 per cent.; captains and first lieutenants, 67.72 per cent.

Promotion to the grades of major, lieutenant colonel, and colonel is by seniority, subject to examination.

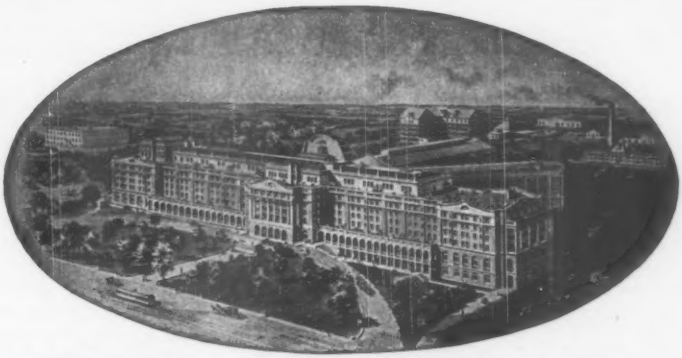
The Surgeon General, who, under the permanent law, has the rank of brigadier general and is the chief of the Medical Department, is selected from among the officers of the Medical Corps not below the grade of lieutenant colonel.

PAY AND EMOLUMENTS

To each rank is attached a fixed annual salary, which is received in monthly payments, and this is increased by 10 per cent. for each period of five years' service until a maximum of 40 per cent. is reached. A first lieutenant receives $2,000 per annum, or $166.66 monthly. At the end of five years *(during the period of the war, at the end of one year)* he is promoted to captain, subject to examination, and receives $2,400 a year, with an increase of 10 per cent. after five years' service, making $2,640, or $220 per month. After 10 years' service the pay would be $2,880 annually, or $240 per month. The pay attached to the rank of major is $3,000 a year, which, with 10 per cent. added for each five years' service, becomes $3,600 after 10 years' service, $3,900 after 15 years' service, and $4,000 after 20 years. The maximum monthly pay of lieutenant colonel, colonel, and brigadier general is $375, $416.66, and $500, respectively. Officers, in addition to their pay proper, are furnished with allowance of quarters according to rank, either in kind, or, where no suitable Government building is available, by commutation; fuel and light therefor are also provided. When traveling on duty an officer receives mileage for the distance traveled, including the travel performed in joining first station after appointment as first lieutenant. On change of station he is entitled to transportation for professional books and papers and a reasonable amount of baggage at Government expense. Groceries and other articles may be purchased from the commissary at about wholesale cost price. Instruments and appliances are furnished for the use of medical officers in the performance of their duties. Well-selected professional libraries are supplied to each hospital, and standard modern publications on medical and surgical subjects, including medical journals, are added from time to time. At each military post there is also a laboratory, and medical officers are encouraged to carry on any special line of professional study which appeals to them and which fits them for their duties as medical officers.

Officers of the Medical Corps are entitled to the privilege of retirement after 40 years' service, or at any time for disability incurred in the line of duty. On attaining the age of 64, they are placed on the retired list by operation of law. Retired officers receive three-fourths of the pay of their grade (salary and increase) at the time of retirement.

At the present time there are approximately 700 vacancies in the Medical Corps.



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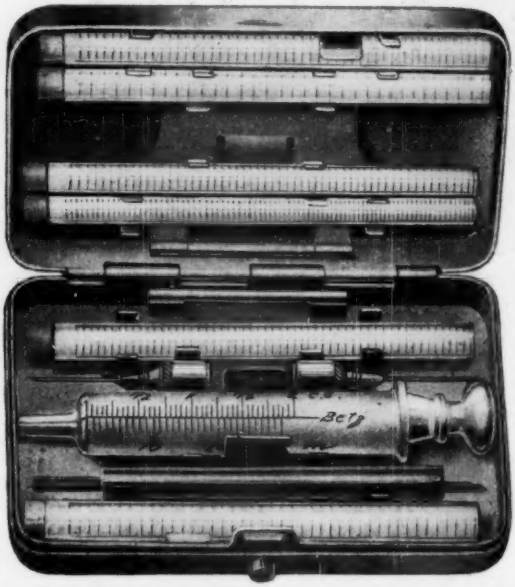

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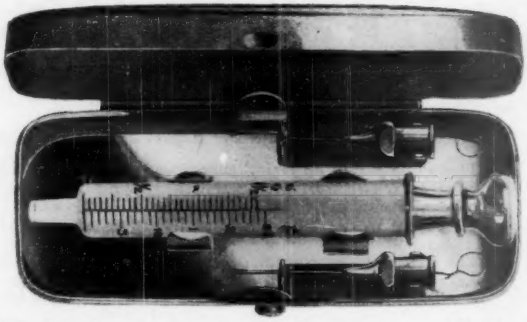

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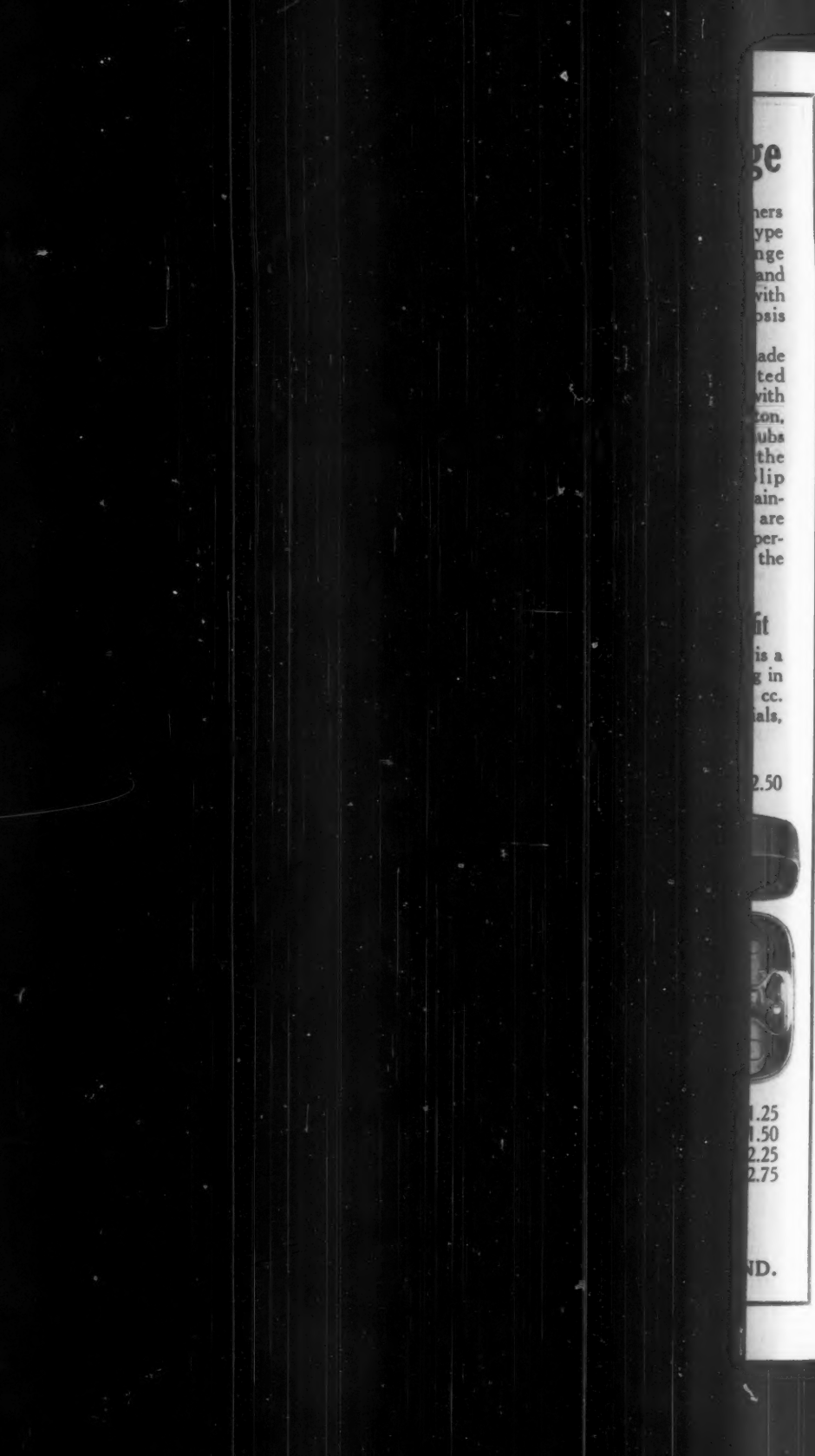

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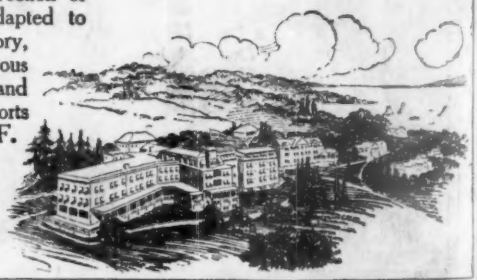

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